Study Protocol and Statistical Analysis Plan

STELLA-FTD: Examination of a Behavior Change Intervention for FTD Family Care Partners

[NCT ID not yet assigned] Unique Protocol ID: 26023

10/20/2023

Minimal Risk Protocol Template

1) Protocol Title

STELLA-FTD: Examination of a Behavior Change Intervention for FTD Family Care Partners

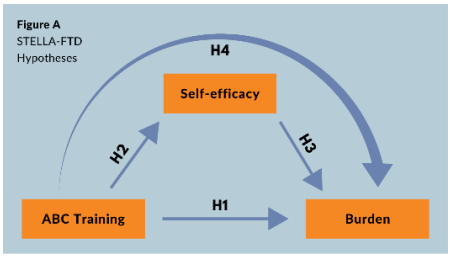
2) Objectives

The purpose of this study is to test the STELLA-FTD intervention that we designed from our pilot study, STELLA-FTD, Phases 1 and 2. The STELLA (Support via Telehealth: Living and Learning with Advancing Alzheimer's Disease)-FTD intervention to specifically address the needs of family care partners of persons with frontotemporal degeneration (FTD). STELLA-FTD is a multicomponent video-conference based intervention designed to facilitate effective use of community and peer resources to foster effective management of behavioral and psychological symptoms of dementia. In the STELLA-FTD intervention, professionals ("Guides") meet with family members ("Care Partners") caring for persons with FTD conditions. Working together, the Care Partners and Guides identify strategies to address upsetting behaviors. The goal of this intervention is to reduce upsetting behaviors and thus care partner burden. **In this study, we will test STELLA-FTD, to specifically address the needs of family Care Partners for persons with frontotemporal degeneration.**

The Specific Aims are:

Aim 1: Test the preliminary efficacy of STELLA-FTD in this **NIH Stage 1B** [(1)] clinical trial by comparing burden on the primary outcome measure, *reactivity* on the Revised Memory and Behavior Problems Checklist (RMBPC)[(2)], between two care partner groups: the test group, who receives training in the ABC analytic approach and the control group that does not.
H0: There will be no change on the RMPBC reactivity score in the two pre-intervention assessments (completed at weeks 1 and 4) in both test and control groups.
H1: Upon completion of the STELLA-FTD intervention, care partners in the test group will have significantly lower (better) burden scores than those in the control group.

Aim 2: Test the **mechanism of action** of STELLA-FTD by isolating the ABC training component (the behavior change technique) and determining its relationship to self-efficacy [(3)] (the intervention target) and burden (the primary outcome) [(2)] (Figure A).
H2: Care partners who receive STELLA-FTD with ABC training (test group) will have significantly higher self-efficacy scores [(3)] than the control group.
H3: Care partners with higher self-efficacy will have lower burden scores.
H4: Self-efficacy will partially mediate the relationship between ABC training and burden.



Aim 3: Prepare STELLA-FTD for NIH Stage 2 testing: standardize materials and fidelity assessment processes.

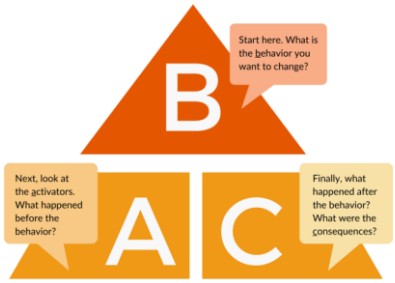
3) Background

Importance of FTD and care partner burden. Dementia due to frontotemporal neurodegeneration (FTD) affects adults at the apex of their work and family life, with the peak incidence between the ages of 45 and 65 [(4)]. FTD disorders are a heterogeneous group of dementias characterized by progressive impairments in behavior, language and motor function due to degeneration in brain regions responsible for executive function, social comportment and language [(5-8)]. FTD includes several subtypes, the most common are behavioral variant frontotemporal dementia (bv-FTD) and primary progressive aphasia (PPA) [(4-6, 8)] (in this proposal, **we group all FTD dementias together and use the term, "FTD").** The combination of behavior and language deficits causes substantial burden for the persons caring for those with FTD, *the family care partners* [(8, 9)].

Care partners report burden in all types and phases of FTD. In the early stages, memory is often preserved, contributing to diagnostic confusion and delay with accompanying family stress and frustration [8, 10-13]. With disease progression, behavioral symptoms such as irritability, anxiety, agitation, apathy and disinhibition become more prominent, predicting higher levels of care partner burden [8, 13]. Behavioral symptoms occur in all FTD types, but tend to happen at different phases in the disease trajectory. For example, in bv-FTD, behavioral symptoms are prominent early on, but in PPA, the symptoms are more pronounced in the later stages. Along with the behavioral changes, language, motor and global cognitive deficits further contribute to care partner burden [6, 8, 11]. Of note, the FTD-related symptoms and their impact on daily and social function lead to care partner burden that is considered greater than that experienced by those who care for family members with Alzheimer's disease [10].

FTD care partner burden is important because it contributes to multiple negative care partner outcomes, including depression, anxiety, social isolation, exhaustion, pre-death grief and impairments in physical and financial health [9, 10, 14]. Families report persistent worry about symptomology and care needs, as well as feeling ill-prepared to manage their family member's future physical, language and social needs. The literature reveals that families need and want education and guidance to facilitate effective symptom management across the disease trajectory [10, 11, 15, 16].

Figure 1. The ABC Pyramid



The Problem. Despite the fact that behavioral symptoms predict significant care partner burden across all FTD subtypes [8, 13], **no interventions, to our knowledge, exist to help FTD care partners analyze and manage behavioral symptoms.** Further, although families ask for help in managing symptoms and preparing for future challenges, few interventions exist that incorporate rehabilitation care to manage the advancing behavioral, communication, physical and social FTD-related changes, despite the World Health Organization's (WHO) mandate that rehabilitation care be a core component in FTD treatment [10, 17]. Families can receive help from support groups offered by national organizations, such as the Alzheimer's Association [18] and the Association for Frontotemporal Degeneration (AFTD) [19]. However, support groups do not provide formal behavior management training and care partner engagement in programs is hindered by access and cost [20-23], particularly for underrepresented, rural and younger families.

The literature reveals that interventions for care partners are being tested, but these do not specifically address behavioral symptoms, they limit enrollment to a specific FTD subtype, have limits on accessibility and/or lack power to identify significant findings. For example, a current online intervention that plans to enroll 90 participants is limited to PPA care partners only and focuses primarily on communication [24]. Another online asynchronous intervention (tested with 61 care partners) was focused on partners of those with young-onset dementias [25]. Use of their online platform was limited, and while findings showed some improvement in burden [2], the study was not powered for efficacy. Neither intervention offers in-depth training on behavior management strategies. A third small RCT engaging 20 care partners of all FTD subtypes addressed behavioral symptoms and engaged occupational therapists in their intervention. However, their intervention involved home visits with no remote access options [26].

The critical barrier this proposal addresses. There is a critical gap in accessible, behavior-focused interventions for FTD family care partners. The National Alzheimer's Project Act Advisory Council calls for development of programming for families living with FTD [27, 28] and care partners in our pilot asked that we **"please do something"** [15] to address their needs, but to date, *no behavior-focused intervention is broadly available for FTD care partners.*

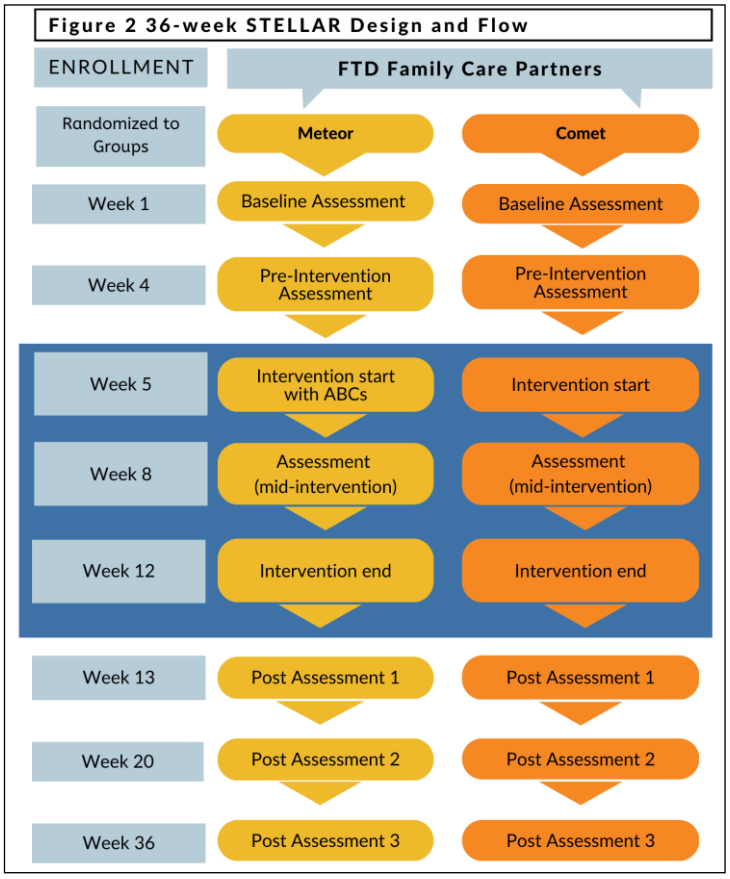
To address this critical gap, we translated an ABC-based intervention for ADRD care partners [29, 30] into an FTD-focused intervention. The revised intervention, STELLA-FTD (Support via Technology: Living and Learning with Advancing FTD) is a telehealth-based, behavior change intervention

designed with and for family care partners of those with FTD. With funding from the AFTD, we pilot-tested the NIH Stage 1A [1] STELLA-FTD intervention and found that it is feasible and acceptable to care partners and has the potential to reduce burden. In STELLA-FTD, care partners are instructed to use the ABC analytic approach to describe a distressing behavior, then identify its activators and consequences (Figure 1). With this information, care partners can develop plans to reduce behavioral symptoms. The STELLA-FTD curriculum is informed by rehabilitation science to support care partners' efforts to address their family members' behavioral, physical and communication needs. As a telehealth intervention, STELLA-FTD is especially relevant to FTD families, given the challenges of traveling or finding respite care for in-person interventions.

How this clinical trial advances scientific understanding of behavior-focused interventions. Since the early 2000s, researchers have employed the ABC analytic approach to address dementia-related behaviors [30]. Building on Teri's work [30], our team and others [29, 31-37] have found quantitative evidence that these interventions reduce care partner burden. However, the *mechanism of action* of ABC-type interventions, including STELLA-FTD, is not well-understood. To our knowledge [38], none of these studies has examined the critical components within the intervention that produce improvements in care partner outcomes. That is, the essential ingredient in these interventions has not been examined or explicated. *The knowledge gained from this study will advance the scientific understanding of how and why ABC-type interventions, and STELLA-FTD in particular, facilitate effective management of behavioral symptoms.*

4) Study Design

STELLA-FTD is a 36-week randomized controlled, repeated measures study. Embedded in it is an 8-week care partner behavior change intervention, delivered in a peer environment via videoconferencing technology. All interactions are completed by telephone, real-time videoconferencing, asynchronous website access and electronically-administered assessments. There are no in-person activities. Importantly, STELLA-FTD is administered via a telehealth platform, ensuring that it is *accessible* to any care partner with internet access, including underrepresented and rural families. All STELLA-FTD activities (e.g., screening, enrollment, intervention) will be managed by the Oregon Alzheimer's Disease Research Center (OADRC) team at OHSU. STELLA-FTD will be monitored by the OHSU IRB, adhering to the highest ethical and regulatory standards.



Rational for intervention study design. To test our hypotheses we will use a randomized controlled, two-group, repeated measures design (Figure 2). This design was chosen to maximize internal validity and address the shortcomings noted in the STELLA-FTD pilot that affected rigor: the quasi-experimental design, insufficient power and no examination of mechanism of action.

Two groups are needed in this intervention to test the mechanism of action and isolate the effect of ABC training. To do this, we designed the intervention so that both groups receive the matching "dose," of the foundational curriculum. The test group will receive the foundational curriculum *plus* ABC training. Comparing differences between the groups will allow us to assess the effect of ABC training (see **Intervention**).

We considered having a "standard care" group instead of the dose-matched group, but because the two groups would receive very different interventions, this would not inform us of the effect of ABC training and ultimately, the mechanism of action.

This design will allow us to assess the effect of the process variables (use of ABC planning, self-efficacy) on the primary outcome variable, care partner burden, while controlling for selection bias and diffusion of treatment [39].

Rigor, bias and transparency. Unlike the quasi-experimental design used in our pilot, the repeated measures RCT described here will provide evidence for efficacy, allow isolation of the active components of the intervention and limit bias [40]. The study will be powered to identify the effect size of the intervention.

We will employ multiple strategies to minimize threats to internal validity and mitigate bias. First, all enrolled care partners will be randomized to the test or control group of the intervention allowing for comparison between and within groups. Care partners will be blinded to group designation.

Second, to limit diffusion of information between the two groups there will be no study-driven opportunities for the test and control group care partners to interact. The telehealth modality uniquely allows for siloed training sessions that do not include in-person interactions (e.g., they will not meet in a hallway or waiting room). While both groups will have access to the STELLA-FTD website, there will not be a chat option to interact. We will engage separate interventionists and handbooks for each group. Nominal names for each group reduce the risk of valuing one group over the other [39].

Third, we balanced the need for frequent testing with the possibility of re-test bias by designing multiple-week gaps between testing. To limit social bias, assessments of burden and other variables (see "Measures") will be electronically delivered to each care partner's email so they can complete them in the privacy of their homes. Staff members will not administer these assessments. Finally, careful adherence to fidelity practices (see **Fidelity**) will limit intervention drift from the protocol.

Our methods, protocol and findings will be transparent to the wider community. STELLA-FTD will be posted on the ClinicalTrials.gov website. We will publish our protocol, training and fidelity procedures and findings to promote reproducibility of the study. We will deliver our findings to the participants and other care partners to honor their contributions.

Sample size calculation/power analysis. A known weakness on the STELLA-FTD pilot was the small sample size. For the proposed study, we will engage a sample of care partners that will be large enough to identify statistically significant findings. To our knowledge, STELLA-FTD is the **first study of its kind** to test an ABC-type behavioral intervention with a large group of **FTD** family care partners. Thus, the power analysis for STELLA-FTD is hampered by the lack of larger-scale studies. We therefore calculated the power based on published ADRD behavioral research that used our primary outcome variable, reactivity on the RMBPC [2, 30, 41].

In Teri et al. [30] the differences in RMBPC reactivity scores [2] between baseline and post-intervention visit were -1.6(SD=7.6) with an effect size of 0.21 in care partners in the control group (routine medical care), and -5.8(SD=9.8) with an effect size of 0.59 in care partners in the intervention group (the ABC group). The effect size of difference in change in RMBPC [2] reactivity score between the two groups was 0.38. Based on this study, we conservatively determined the sample size calculation with an effect size of difference in pre-post intervention change as 0.3. To achieve at least 80% power to detect such a difference in a study design with three repeated measurements and an Intra-Class Correlation (ICC) =0.5 to 0.6 in compound symmetry covariance structure, we need at least 117 to 128 subjects/each group, for alpha = 0.05.
We anticipate an increase in power due to our conservative approach, e.g., based on three time repeated measures instead of 6 time points (Figure 2) and smaller effect size between intervention

and control groups on the RMBPC (compared to 0.59 Teri et al.) [30]. We will use this increase in power to compensate for the complexity of the proposed model when adjusting covariates are taken into consideration. For self-efficacy, based on estimates from the STELLA-FTD pilot, group sample sizes of 128 will achieve 80% power to detect a difference of 0.32 at alpha level of 0.05, which is reasonable given pilot data trends [42].

In determining the sample size, we took attrition into account. Based on our experience [29], it is likely that up to 15% of the sample will withdraw due to schedule demands, illness and death, thus we will over-recruit to enroll 300 care partners.

5) Study Population

a) Number of Subjects

Participants. Informed by our power analysis, we will enroll a total sample of 600 participants: 300 family care partners and their 300 care recipients with FTD. For our study "family care partner" includes any person who is considered "family" to the person with FTD, such as direct relations, fictive kin, close friends and neighbors. "Care recipient" is defined as an individual with an FTD diagnosis: bv-FTD, PPA, progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), or FTD with motor neuron disease [43].

Care recipients with FTD will **not participate in intervention** but will be consented (and thus enrolled) because we will collect data about them (e.g., demographics, diagnosis). Further, it is possible they may enter the videoconferencing space during intervention and their privacy may be compromised. We have used this approach in our other studies [29, 33, 34], resulting in a transparent process that recognizes the agency of the individual with FTD and adheres to high ethical standards.

b) Inclusion and Exclusion Criteria

The criteria are informed by our previous work [29, 33, 34] in which the majority of care partners had a good fit with study goals. For STELLA-FTD all participants will be adults over the age of 18 (FTD does not affect children 18 and under) who live in the United States. Family care partners must speak English and have adequate vision and hearing to participate in trial activities. Care partners must provide at least four hours of care/week to the individual with FTD. Care partners need to have a telephone, internet access and be willing to participate in the videoconference-based meetings. They need to have an email address to receive study materials and assessments. Care Partners must document at least two behaviors, in the person with FTD, that distress them, such as Care Recipient pacing or yelling.

To be included in STELLA-FTD, care recipients must have a diagnosis of FTD as defined above, by self or care partner report. We considered verifying the diagnosis with the participants' medical providers; however, in our experience, this deterred some potential participants and caused substantial delays [33]. We considered limiting the sample to a single diagnosis (e.g., PPA or bv-FTD), but behavioral symptoms occur in all FTD subtypes [8]. We learned from our pilot, in which care partners had family members with bv-FTD, PPA and PSP, that the care partners liked learning from each other. In post-pilot focus groups, care partners recommended STELLA-FTD include all FTD diagnoses. Further, because FTD dementias are rare, we need broad inclusion criteria to meet our sample size goals.

Care Partners need to provide care for their family member with FTD, but this care does not need to be in-person. Care Partners experience burden regardless of the location of the person with dementia, thus they do not have to live with them (Table 1). Care Partners who attend an external support group can participate. Care partners must consent to be video-recorded while in STELLA-FTD sessions. They may turn off their cameras if they prefer.

Exclusion Criteria, Phase 2. See Table 1 for detailed Inclusion/Exclusion Criteria. It should be noted that this study includes Care Partners for those with advanced FTD. Thus, it is possible, but not likely, that the care recipient with FTD will die of natural causes while in STELLA-FTD. If this occurs, the Care Partner will be excused from the study.

Table 1. Inclusion/Exclusion Criteria, STELLA-FTD Phase 2

Participants	Inclusion	Exclusion
Care Recipient	• Diagnosis of FTD or FTD-like dementia. • Family member of Care Partner (this can be a relative, spouse, or close kin that is considered family). • Live in US	• No Frontotemporal Degeneration diagnosis. • Unable to leave Care Partner during STELLA-FTD sessions.
Care Partner	• Adult caring for family member with FTD-like dementia. • Provides 4 or more hours of care/week • Speaks and understands English to be able to participate in intervention. • Owns a telephone (smartphone, cell phone or landline). • Has email and mailing address to receive computer, study materials and surveys. • Provides informed consent to participate in the research.	• Unable to find activity for care recipient during STELLA-FTD sessions to allow Care Partner to work privately with Guide and other Care Partners. • Hearing and/or vision problems severe enough to prevent participation. • Refuses to be video-recorded during STELLA-FTD sessions. • Unwilling or unable to adequately follow study instructions and participate in study procedures.

Once identified, the recruitment team will complete the full screen with potential participants, and if eligible, proceed with the consent procedures (below) with the eligible Care Partners. Screening will be completed using paper or electronic (Qualtrics or REDCap) forms.

In the event of a screen failure, data collected during screening will be destroyed at the end of the study. The recruitment team will track the number of Care Partners screened for the study, the number consented, the number of those that dropped out, the number who completed some of the intervention, and the number of those that completed the entire intervention.

c) Vulnerable Populations

The primary focus of this study is to assess the efficacy and mechanisms of action of the STELLA-FTD intervention. Therefore, in order for this study to be successful, Care Partners of care recipients with FTD will be enrolled. The care recipients (the persons with FTD), who will likely be decisionally impaired, will also be enrolled.

There is a risk of loss of confidentiality if the persons with FTD come into view of the Care Partner's computer screen or if they are overheard on the audio during the STELLA-FTD sessions. Care Partners may discuss their family member with behaviors with other study participants. It may be distressing for the person with FTD if they overhear their Care Partner discussing their family's situation.

To minimize these risks, we will ask Care Partners to identify an activity that will keep the person with FTD (and anyone else) occupied and out of computer range during the weekly, hour-long STELLA-FTD visits. Please see Decisionally-Impaired Adult Worksheet.

d) Setting

This study will occur at OHSU. All study activities (screening, consent, intervention, surveys, etc.) will be conducted by the OHSU team.

All study activities will occur via phone, videoconferencing, mail, or encrypted email. No in-person visits are required.

Care partners will participate in the study from their own homes (or other private location), which may be anywhere in the United States.

e) Recruitment Methods

We will recruit nationally for STELLA-FTD, engaging multiple strategies, from in-person promotion to wide-spread social media use. We will recruit from our Oregon ADRC and the other 33 ADRCs around the nation. The Oregon ADRC's studies include the African American Dementia and Aging Project, the Clinical Core and the Digital Technology Core. Combined, these cohorts have about 400 participants, with 13% from underrepresented groups.

Our pilot funder, the AFTD, will promote the study and assist us with contacting FTD support group leaders. In addition, we have secured permissions to recruit from three national entities: the ALLFTD study, The FTD Disorders Registry and the RISE registry. These registries will facilitate recruitment of multiple care partners from diverse backgrounds (e.g., race [44], rural [45] and sexual and gender minority individuals [SGM] [46]).

The ALLFTD is a nationwide study that focuses on characterizing FTD conditions, collecting cognitive, clinical and diagnostic data and sharing data with scientists [47]. The ALLFTD study currently includes 1,021 individuals with FTD, of which 51.5% are female. Most (96.8%) are non-Hispanic and White (94.5%), 1.5% are Black and 2.6% are Asian [48]. The ALLFTD co-investigator, Dr. Howard Rosen, is a collaborator on STELLA-FTD and will facilitate recruitment from ALLFTD with the help of a staff member.

The FTD Disorders Registry has 5,719 registrants, of which 23% (1337) carry a diagnosis of FTD. The registry also lists care partners (n=1,935) [43]. We will post our study with the Research Inclusion Supports Equity (RISE) Research Registry to promote inclusion of SGM care partners (5R24AG066599). The RISE Registry has 376 individuals, of which 5% identify as gender non-conforming and 6% identify as queer. This sample is racially diverse with 61% identifying as Black and 27% Hispanic [46].

The STELLA-FTD team will learn of interested parties in several ways:

- A clinic, registry, or other resource will provide contact information (phone, email) to the OHSU STELLA-FTD team via a secure OneDrive file, or via telephone to the STELLA-FTD RA.
- Interested parties will respond to our social media advertisements
- Interested parties may telephone, text or email us (once we make contact we will explain that email and text are not secure and should not be used).

Respondents to the media or other contact (e.g., clinic patients, referrals from clinicians or calls from the AFTD) will be contacted to collect basic information about eligibility. They can complete this "pre-screen" via phone, or via an electronic screening survey, providing their names and contact information, the family member's diagnosis (see Screening Survey). This brief survey provide enough information to inform the study staff if further screening is needed. Interested respondents must provide their contact information if they would like the team to contact them.

If the potential participant meets the pre-screening criteria, the study RA will meet with them via phone or video for a more detailed screen. This screen provides enough information to ascertain if the potential participant is eligible. The screening process will not adversely affect the rights and welfare of the potential subjects. Following OHSU screening protocol, we will seek their verbal permission to screen them. Prior to other questions, we will review their right to privacy and OHSU phone numbers will be provided. If they are not eligible, the pre-screen form and all data will be deleted. Please see HIPAA Waiver request.

If the potential participant is eligible, they will be automatically connected to the eConsent. Screening data may be stored on Excel files on the OHSU OneDrive, the H or X drives and/or the Qualtrics and REDCap databases.

f) Consent Process

Eligible participants will be directed to an online eConsent. The eConsent describes the study in detail. The eConsent provides details about the study and has questions the confirm understanding. If the participant's answers indicate poor understanding of the eConsent, the RA will contact them to review. Upon completing the eConsent, participants will provide their intitials to attest they have reviewed the consent. The participant will retain a copy of the eConsent; the STELLA-FTD study will not retain copies of the eConsents. The eConsent can be accessed on a computer, smartphone, or other device. At the first STELLA-FTD session, the PI will review the key points of the consent with the participants.

Participants will be advised that the study team is obliged to report any elder abuse. Participation in this research is not meant in any way to replace regular care.

We will also collect an eConsent for person with FTD because we will collect data about them and if they enter the recorded sessions, their privacy may be compromised. If the person with FTD is not capable comprehending eConsent we will seek consent from their legally authorized representative [49, 50]. If the person with FTD is capable of consenting and does not consent, their care partner cannot participate in STELLA-FTD. Consent forms will contain information about data sharing and management, per NIH policy. [51] All consent processes will be approved and monitored by OHSU IRB.

Due to the complicated nature of FTD conditions, the potential subjects' decisional impairment many be intermittent, progressive, or complete.

Once a care partner is deemed eligible for the study, and prior to the care recipient's consent, we will ask the family care partner these questions (either on a videoconference call or survey).

Do you think your family member would be able to provide consent for this study? The person with dementia would need to do the following:

i. Talk with the STELLA-FTD staff on the phone for about 30 minutes to review the consent form
ii. Understand the risks and benefits
iii. Make an informed decision about whether or not he or she would like to consent

If the family care partner does not think the person with FTD can meet these criteria, we will ask the family member to have the LAR review the consent form and consent on behalf of the person with FTD.

We ask the care partners if they are the legal authorized representative. If yes, the team will document this and proceed with send them the eConsent for the care recipient.

If the care partner is not sure they are the LAR, the RA will read this list to see if they meet the criteria:

1) Health care representative who is legally authorized by a valid advance directive or health care power of attorney
2) Court-appointed guardian
3) If the above two do not exist or cannot be located with reasonable effort, another surrogate who knows and can represent the previously expressed wishes of the potential subject, in the following order of preference:
a) Spouse or registered domestic partner
b) Adult child
c) Either parent
d) Adult sibling
e) Adult designated by others on this list, if no one on the list objects
f) Other adult relative or friend who has an established relationship with the potential subject.
If the LAR is not the care partner, ask the care partner to please contact the LAR to arrange for them to be present during the consent appointment.

If the person with FTD is not able to consent, their eConsent will be emailed to the care partner. The care partner will be advised to review with the care recipient if possible. The care partner will sign for the person with FTD.

FTD is a progressive disease. Participants will not regain the capacity to consent as the study progresses.

The person with FTD will not have any role in the study. We will only collect information about them. Because there is a risk of loss of confidentiality if they enter the room during the video sessions, we are seeking their consent.

Please see Decisionally Impaired Adults Supplement for details of consenting persons with FTD.

6) Procedures

Enrollment and Set-up. After consenting to the study, Care Partners will be contacted by the study research assistants (RA) to collect enrollment information (e.g., demographics, contact information) and orient them to logging on to the STELLA-FTD on their computers (see "Technology" below). The RA's will mail the "STELLA-FTD" Care Partner Handbook" and ClinCard to the Care Partner, which provides details about all study activities.

Randomization. Care partners will be randomized to either the test or control group (Figure 2) using an electronic randomization process and will be blinded to their group designation. The control group ("Comet") will receive the basic STELLA-FTD curriculum, the test group ("Meteor") will receive the basic curriculum *plus training in the ABC analytic approach*.

Interventionists. The STELLA-FTD intervention is provided by "guides," health care professionals (e.g., Speech and Language Pathologists, nurses) with experience in dementia care. There will be two guides for each group per 8-week cohort, for both control and test (see "**Fidelity**," for training information).

Technology. STELLA-FTD is a technology-based intervention. We have been conducting telehealth-based care partner research since 2016 [15, 24, 29, 31, 33, 34, 41, 42, 52] and our experience informs delivery of STELLA-FTD in a safe, acceptable manner. The intervention, assessments and all communications will be delivered by electronic, videoconference, or by telephone strategies. The consent form will explain technology and privacy risks.

Participant Communication. All contacts, surveys and interventions may be completed by phone, encrypted email, videoconferencing and/or electronically-administered assessments using REDCap or Qualtrics servers. All other study activities (screening, consenting, intervention and surveys) will be done at OHSU by OHSU scientists, interventionists and staff. There are no in-person research activities. We will send occasional newsletters with study updates use OHSU Marketing Cloud. The OHSU Marketing Cloud has been approvied by the OHSU Director of Internal Communications, and there is a Business Associate Agreement in place for handling of PHI.

Care partners will have the option of opting out if they do not want to receive the newsletters.

The intervention will be delivered synchronously through a videoconference interface and augmented by asynchronous access to the STELLA-FTD website. The website will be designed with the Oregon Clinical and Translational Research Insitute (OCTRI)Center. The domain for this website will be hosted via an OHSU domain: likely octri.ohsu.edu/stella-ftd. OCTRI will develop and host the web application which will be hosted in the OHSU Data Center West and assisted by ACC. OCTRI routinely updates and patches applications and servers in accordance with OHSU Information Security Directives. We attempt to adhere to all OHSU ISDs and review all directives annually.

OCTRI will collect the websites metrics and record the information locally. They will not rely on any third-party system for metrics

There will be no third parties involved in the development or hosting of the application

The website will require HTTPS (TLS 1.2), and data is encrypted in transit within the OHSU network, as well.

Care partners will access STELLA-FTD sessions using OHSU's secure videoconferencing link. Staff will be available during the sessions to provide technological support. We use this strategy in our current study [29], in which, of 350 visits, only 3% (to date) have had moderate technology problems.

Assessments (see **Measures**) will be administered via the REDCap platform [53], or Qualtrics. Both provides secure, easy-to-use assessments that care partners can complete on their laptop, device or phone. Data will be stored on a secure server. Study staff will ensure that all data are collected, maintained and stored in password-protected databases at OHSU.

Each STELLA-FTD participant will have access to the STELLA-FTD technology support team. This team has extensive experience in working with individuals who are technologically naïve and/or are overwhelmed by their caregiving work. The team excels in providing thoughtful support while setting up the care partner's access to the study, facilitating high-quality sessions or troubleshooting older equipment. They will test the participants' access to the videoconferencing sessions. If all attempts fail to connect the care partner to the sessions, the care partner can join the sessions via phone. This is the practice in our current study, where fewer than 4% need to connect by phone only [29].

Materials. All care partners will receive group-specific handbooks (Appendix A) [54], *The FTD Roadmap*© (Appendix B) and access to the STELLA-FTD website with instructional resources and videos. The group-specific handbooks (either "Comet" or "Meteor") [54] provide information on FTD and the weekly lessons. *The FTD Roadmap*©, designed and tested in the STELLA-FTD pilot, provides information on services that can support families throughout FTD disease progression. The materials will be sent to all care partners after they have completed the week 4 pre-intervention assessment. Care partners may keep their materials. Over the course of the study we will seek feedback from care partners about the utility of the materials (see Measures), and revise them for a future Stage 2 study[1].

The STELLA-FTD website will have two components: written instructional resources and recorded videos. Rehabilitation specialists and other professionals with experience working with FTD families will create one-page written educational documents and record 15-minute videos about how their specialty can help address current FTD symptoms and prepare for future needs. This information will align with the visual markers on *The FTD Roadmap*©. Care partners will access the videos on the private STELLA-FTD website with their user ID and password and can watch the videos whenever they need to, even after they have completed STELLA-FTD. We will monitor engagement with the website, in which metrics will provide robust objective data, indicating how often participants log in and view the resources and videos.

Box 1. STELLA-FTD Basic Curriculum Topics (Specialist)

- FTD Basics (Nurse)
- Caring Tasks and Challenges (Occupational Therapist)
- Communication (Speech Language Pathologist)
- Care Partner Well-being (Social Work)
- Exercise and Balance (Physical Therapist)
- Advanced Care Planning (Elder Law Attorney)
- Nutrition (Dietician)
- Staying Connected post STELLA-FTD (Nurse)

The Intervention: How the study includes the hypothesized mechanism of action. We hypothesize that STELLA-FTD's mechanism of action involves training in the ABC analytic approach (the behavior change technique). The training increases care partner self-efficacy (the intervention target and mediating variable), that results in decreased burden (the outcome variable) [55]. Here we describe the training method.
The STELLA-FTD intervention is delivered over 8 weeks in 1-hour "live" video-based group sessions led by two guides. There will be two intervention groups, the control group ("Comet") and the test group, ("Meteor") (Figure 2). There will be up to 8 care partners per group, which allows for the development of mutual trust and commitment [56].

The Basic Curriculum. The basic STELLA-FTD curriculum "dose" will be provided to all care partners (test and control). The curriculum was informed by pilot testing and involves 8 lessons on topics about care challenges and resources for families. This multi-modal curriculum includes synchronous video-based instruction about FTD as well as the asynchronous access to the weekly video and written materials. During the sessions, explicit knowledge acquisition [57] will be facilitated as the guides highlight key points of the video, encourage interaction between care partners and discuss use of their handbooks. The STELLA-FTD-Basic group will receive the basic curriculum only.

Meteor Curriculum. The Meteor group will receive the basic curriculum **plus explicit training in the ABC analytic approach** to address their care recipient's distressing behaviors. The ABC training will occur within the context of the basic curriculum (**Box 1**), so all care partners will receive information about FTD and supportive services (see **Box 2** for example case).

Using the scaffold of the ABC pyramid (Figure 1), guides will train care partners to fully define the behaviors they want to address by observing, describing, and writing about them. The care partners will then be taught to identify the activators, the triggers for the behaviors. Next, care partners will be taught to consider what happens after the behaviors, the consequences. With this information, care partners can develop, write and test personalized ABC plans using the forms in their handbooks. Care partners will be encouraged to share their ABC plans with their peers in the video-based sessions.

The inclusion of training in the ABC analytic approach in the STELLA-FTD+ABC group incorporates theory-based training to promote care partner self-efficacy in managing the FTD-related behavioral symptoms in four important ways. First, care partners will be trained in the ABC approach and instructed to actively use their ABC plans--to write them down, share their ideas with the group, note their successes and modify the plans as needed. Second, care partners will be advised to translate their ABC plans into action by testing them with their family members with FTD. Third, guides will use strength-based feedback to validate and reinforce care partner efforts; and fourth, peer interaction will allow care partners to witness the trials and successes of other care partners. These strategies provide progressive opportunities for success, which, according to Bandura, is essential to building self-efficacy (the intervention target), translating knowledge into action and ultimately, reducing care partner burden (the outcome variable) [58].

Box 2. Hypothetical example case: Differences between groups

The Behavior

A care partner is frustrated with her family member's behavior of yelling at her.

STELLA-FTD-Comet

The care partner receives the Basic Curriculum along with her peers. The sessions (Box 1) include information on FTD and instructions from specialists about common caregiving challenges. The care partner is taught how to use the FTD Roadmap© to identify supportive services and she is encouraged to write notes in her *STELLA-FTD Handbook*.

STELLA-FTD Meteor

The care partner receives the Basic Curriculum *plus* training in the ABC analytic approach. By working through the ABCs, she learns that when she asks her family member questions in an attempt to engage him (the activator), he becomes frustrated by his poor word-retrieval/limited fluency and thus yells at her (the behavior). They are both frustrated (the consequence). She writes her observations in the *STELLA-FTD+ABC Handbook*, brainstorms with her guide and peers on ways to address the communication challenges and refers to *The FTD Roadmap©*. Her detailed written ABC plan includes modifying how she asks questions and securing a SLP referral. The instruction and practice in use of the ABC analytic approach boosts her sense of self-efficacy and she is confident she can try this plan to address both the yelling and her frustration.

To assess enactment of the ABC analytic approach guides will directly observe care partners in group discussion regarding their use of their ABC plans and how they applied them to their target behaviors. To verify receipt of the intervention, guides will query care partners about application of their ABC plans and we will collect the data from their ABC plans to identify changes in behaviors. Care partners will record the number of ABC plans they developed each week in a weekly survey [59] (see also "**Measures**" and "**Fidelity**" below).

How the intervention differs between groups. Both groups (test and control) will receive the basic curriculum. The test (Meteor) group will receive, in addition, ABC training (see **Box 2** for example).

Fidelity. The STELLA-FTD trial utilizes a vigorous fidelity assessment protocol that examines interventionist (guide) adherence to protocols and participant enactment of the intervention (Box 3). We utilize this protocol in our current study [29] to reduce threats to internal validity and facilitate dissemination of findings and procedures . This protocol is informed by evidence-based standards, including recommendations from the NIH Treatment Fidelity Workgroup Behavior Change Consortium [60] and addresses five components. The first three (design, intervention receipt, enactment) are discussed above. Training and delivery monitoring [61] are addressed next.

Guide training. Guides will participate in standardized didactic and experiential training. Best practices in managing and facilitating group sessions will be emphasized. Mock sessions will allow guides to practice group strategies such as management of inappropriate behavior (e.g. use of disparaging comments) and inclusion of reticent participants. Guides will demonstrate essential competencies in behavior identification, intervention delivery and data documentation prior to implementing STELLA-FTD. All

training will be completed via videoconferencing and recorded to maintain consistency across guides.

Delivery monitoring. All STELLA-FTD sessions will be recorded and recordings will be stored on a secure server that the fidelity assessment team can access via the OHSU secure filesharing system. The team will view a randomly-identified subsample (15%) of the recordings to evaluate procedural, documentation and theoretical fidelity. Fidelity items are scored using a binary rating of "1" (present) or "0" (absent), with clearly defined characteristics required for either rating. Inter-rater agreement on video assessments will be measured [62].

Standardized checklists and criteria will be used for each fidelity domain. Guides will be required to complete session content checklists to ensure essential study components are addressed. Session duration will be monitored to prevent potential threats of variance in dosing between trial groups.

We will actively monitor for potential contamination between the test and control groups. Our study design, operationalized procedures and ongoing and diligent fidelity monitoring will aid in early identification and management of fidelity concerns [60].

Taken together, the STELLA-FTD intervention will be implemented within an adequately-powered research design that will test the proposed hypotheses. We will have a fidelity assessment process in place to ensure adherence to protocol. Our intervention will allow us to conduct the trial efficiently and provide interpretable results. To answer our research questions, we will employ relevant measures.

Anticipated challenges. Scheduling Care Partners may be difficult. Thus, the protocol allows the following concessions:

- The study team may alter the session schedules due to holidays, illness or other scheduling issues.
- There may be two sessions may be doubled in a week if scheduling challenges.
- Care Partners can skip up to 3 sessions and still remain in the study.
- If there are more Care Partners than available Guides, the Care Partners may have to wait to the sessions. We will enroll them and have them do the weekly survey until there is space. Four weeks prior to start, they will complete their first set of surveys.

Table 2: STELLA-FTD Care Partner Activities

Activity	Description	Due
Consent	Care Partner and care recipient consent	Prior to any study activities
Randomized to groups	Either test or control group	After consent completed
Assessments	Basline Assessment	4 weeks prior to STELLA-FTD start
Assessments	Pre-Intervention Assessment	1 week prior to STELLA-FTD start
STELLA-FTD Intervention	Meet with Faculty and Guest Speakers for 8 weekly, 1-hour, sessions	1 week after pre-intervention assessment
Assessment	Mid-intervention Assessment	4 weeks after start of STELLA-FTD sessions
Assessment	Post Assessment 1	Within one week of completion of STELLA-FTD
Assessment	Post-Assessment 2	2 months after end of STELLA-FTD
Assessment	Post-Assessment 3	6 months after end of STELLA-FTD
Weekly Orbit Surveys: **Distributed weekly** Orbit surveys start after enrollment and continue until all surveys are completed		

Measures (Table 3). The primary outcome variable, burden, will be assessed with the 24-item RMBPC [2], which measures the frequency of care recipient behavioral symptoms and care partner reactions to these behaviors. The RMBPC was chosen because it aligns with our theoretical foundation that assumes burden is a result of care partner reactions to behavioral symptoms. The RMBPC has been used in Teri's work [30] and our telehealth

studies, [29, 31, 33, 34] including the STELLA-FTD pilot, allowing for comparison across studies.

Self-efficacy, the mediating variable, will be assessed using Fortinsky's measurement of family care partner self-efficacy for managing dementia [3]. We considered the other measures, but Fortinsky's assesses the targets in STELLA-FTD: behavior symptom management and service use.

We will measure care partner preparedness for current and future challenges [63] and personality type to test the effect of a group-based intervention [64].

For care partners in STELLA-FTD+ABC, we will assess the results of the care partners' personalized ABC plans prior to and after the 8-week intervention by collecting data on the frequency of their identified behaviors, and their reactions to them, on their Personalized Target Behavior Survey [29, 30]. We well collect data on number of ABC plans each care partner writes on the Orbit weekly survey, weeks 4-36.

Care Partners may fill out weekly "Orbit" surveys that were developed by the Oregon Roybal Center for CAre Support Translational Research Advantaged by Integrating Technology (ORCASTRAIT), housed at the Oregon Alzheimer's Disease Research Center. The survey includes the "ORCASTRAIT Care Partner Weekly Survey," which measures Care Partner emotional and physical strain, The 4-item ZBI, a brief measure of burden (α=.78),[31] medication use, likelihood of placing their care recipient into long term care (e.g., assisted living, memory care), and frequency of contact with both their and their family member with dementia's clinical providers. Also included in the Orbit survey is the "ORCASTRAIT Caregiver Cost Survey," which measures out-of- pocket costs. The two surveys will take approximately 1-15 minutes (total) to fill out and will be emailed to the Care Partners weekly used REDCap or Qualtrics. Each group (test and control) will receive Orbit surveys specific to their group.

We will use focus groups to seek feedback on the handbooks and *The FTD Roadmap©.* While these materials were developed with pilot feedback, input from a larger sample will provide information on further refinement of the materials to be used in future studies.

Care Partners who are unable to complete all STELLA-FTD components will remain in the study and we may collect the data noted in Table 3. Care Partners who do not complete any trainings, or are unwilling or unable to adequately follow study instructions and participate in study procedures, may be withdrawn from the study. We will retain and analyze any data from their participation. They may also be asked to complete the surveys, despite not completing all of the trainings.

Care Partners may fill out weekly "Orbit" surveys that were developed by the Oregon Roybal Center for CAre Support Translational Research Advantaged by Integrating Technology (ORCASTRAIT), housed at the Oregon Alzheimer's Disease Research Center. The survey includes the "ORCASTRAIT Care Partner Weekly Survey," which measures Care Partner emotional and physical strain, The 4-item ZBI, a brief measure of burden (α=.78),[31] medication use, likelihood of placing their care recipient into long term care (e.g., assisted living, memory care), and frequency of contact with both their and their family member with dementia's clinical providers. Also included in the Orbit survey is the "ORCASTRAIT Caregiver Cost Survey," which measures out-of- pocket costs. The two surveys will take approximately 1-15 minutes (total) to fill out and will be emailed to the Care Partners weekly using REDCap or Qualtrics servers.

If the Care Partners drop out of the study, we will ask them to complete the Exit Survey so we can get their feedback.

Table 3. STELLA-FTD Measures	
Enrollment	
Demographics	Age, sex, gender identity, marital status, race, ethnicity, rurality, etc.
FTD characteristics	Diagnosis, year of diagnosis, daily hours of caregiving
CDR Plus NACC FTLD [6]	Person with FTD disease severity, behavioral & language symptoms (data provided by Care Partner)
Baseline Assessment (Week 1)	
Revised Memory & Behavioral Problems Checklist (RMBPC) [2]	Measure of frequency and reactivity to behavioral and psychological symptoms of dementia, α 0.86
Self-efficacy for symptom management and support service use [3]	10-item scale, α 0.77
Preparedness for Caregiving Scale [63]	8-item measure, α 0.91
Ten Item Personality Inventory [64]	Measures intro- and extraversion (α .45-.68)
Pre-intervention Assessment (Week 4)	
RMBPC [2]	(as above)
Self-efficacy for symptom management and support service use [3]	
Preparedness for Caregiving Scale [63]	
Service and support use survey	
Personalized Target Behavior Survey [29, 30]	Measures frequency and reactivity of up to 3 personalized behaviors identified by care partners
Mid-Intervention Assessment (Week 8)	
RMBPC [2]	(as above)
Post Assessment 1: Same as Pre-Intervention Assessment *Plus*:	
STELLA-FTD contact [29]	STELLA-FTD care partner contact with peers
STELLA-FTD Experience Survey [29]	16-item- survey on satisfaction, privacy, ease of use
Post Assessments 2 & 3: Same as Pre-Intervention Assessment *Plus*:	
STELLA-FTD contact [29]	STELLA-FTD Care Partner contact post intervention
Orbit Survey: **Distributed weekly starting Week 5 [29]:** # of ABC plans (ABC group), service use, burden	

We will implement the above measures using Qualtrics or REDCap Survey Platforms. The surveys will be sent to the Care Partners using these platforms. Auto-reminders will be sent to the Care Partners until they complete the surveys. If they do not complete the surveys within 5 working days, the STELLA-FTD coordinator may call them to identify barriers to completing the surveys. The electronic functionality allows Care Partners to complete surveys in the privacy of their homes, at a time that works for them. The Qualtrics and REDCap platforms are HIPAA compliant and secure. We will assess completion rates and internal consistency of the online platform surveys. Focus group participants will be queried about their experience with the platform.

7) Data and Specimens

a) Handling of Data and Specimens

No biological or genetic specimens will be collected in this study. Data from the measures described above will be collected via the secure Qualtrics or REDCap systems and then downloaded to a secure OHSU file for analyses. Video-recordings of focus groups and intervention sessions to be used for quality assurance and fidelity assessment. Videos not used for these tasks may be deleted. De-identified transcripts of qualitative data will also be downloaded to a secure OHSU file for analysis.

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b) Sharing of Results with Subjects

If the burden or depression scores indicate severe depression or burden, the Care Partner may be informed, at the discretion of the PI. The Care Partner may be referred to appropriate services if deemed necessary (e.g., social worker or other counseling services). The other results may be provided, if asked, after all data is collected, analyzed and published.

c) Data and Specimen Banking

Data from this study may be shared with other investigators for future research studies through the data repository (OHSU IRB # 6845). Data from the repository will be shared with other investigators according to the IRB approved repository policy.

8) Data Analysis

Data Analysis. This study will generate a comprehensive set of data that tests STELLA-FTD's preliminary efficacy and its mechanism of action. In all final models, we will examine the relationships between diagnosis type, demographic and biological characteristics (e.g., sex, race, education) and the outcome and process variables.

Aim 1. *Test the preliminary efficacy of STELLA-FTD in this* ***NIH Stage 1B*** *clinical trial by comparing burden (reactivity on the RMBPC [(2)]), between two care partner groups: the test group, who receives training in the ABC analytic approach and the control group that does not.*

H0: There will be no change on the RMPBC reactivity score in the two pre-intervention assessments (completed at weeks 1 and 4) in both test and control groups. The primary outcome for H0 is the RMBPC [(2)] reactivity score. First, we will provide both statistical and graphical evaluation for the distributions of the primary outcome and transform the data to normalized values if needed (e.g., log transformation). We will descriptively explore the RMBPC [(2)] reactivity score at weeks 1 and 4 for each group and the primary outcome will be reported as mean (SD). To test whether reactivity scores change from week 1 to week 4, paired t-tests will be used to compare scores within each group. Then, we will compute the change scores between week 1 and week 4 for each participant and the normality of change score will be assessed. If normality assumption is violated, we will perform a data transformation. To test the difference in change scores between weeks 1 and 4, we will conduct a two-sample t-test of the change score between the test and control groups. All of the results will be considered significant at $\alpha = 0.05$. We expect no significant change between weeks 1 and 4 within each group and the change scores will not be significantly different between the test group and control group.

H1: Upon completion of the STELLA-FTD 8-week intervention, care partners in the test group will have significantly lower (better) burden scores than those in the control group. For H1, we will employ a mixed effects model to analyze whether the change in reactivity on the RMBPC [(2)] differs across groups (test vs. control) over the intervention period. Two fixed effects will be included in the model: 1) Group effect will be included as a dichotomous categorical variable (test vs. control); 2) Time effect will be included as a continuous variable. The interaction between group and time (group x time) will also be included. Random intercepts will be incorporated for subject specificity in the model to account for clustering effect within subject over time. We will perform a hypothesis test for the coefficient of the interaction term (group x time) to assess the difference in change on primary outcome in the intervention group as compared to control group, over time. We will extend the model to include diagnosis type (e.g., PPA, bv-FTD), frequency of behavioral symptoms as measured on the RMBPC [(2)], socio-demographic covariates (e.g. sex, age, sex, education) and external support group use. Results will be considered significant at $\alpha = 0.05$, with two-sided test. Similar analyses will occur at Week 20 and 36.

Aim 2. *Test the* ***mechanism of action*** *of STELLA-FTD by isolating the ABC training component (the behavior change technique) and determining its relationship to self-efficacy (the intervention target) and burden (the primary outcome) (Figure A).*

The statistical analyses for Aim 2 will be carried out in three steps to investigate the mediated effect of self-efficacy [3] on the association between intervention and primary outcome, the RMBPC [2] reactivity score.

H2: Care partners who receive STELLA-FTD with ABC training (the test group) will have significantly higher self-efficacy scores [3] than the control group. To test H2 in the first step, we will employ a similar mixed effect model as H1. The mixed effect model analyses will be performed on total self-efficacy score as the outcome. A hypothesis test for the coefficient of the interaction term (group x time) will be performed to assess the difference in change on self-efficacy score in the test group as compared to control group, over time.

H3: Care partners with higher self-efficacy will have lower burden scores. In the second step to test for H3, we will construct a mixed effect model on the RMBPC [2] reactivity score as the outcome. Total self-efficacy score [3] will be included as a continuous independent variable; time will be included as a continuous variable. The interaction between total self-efficacy score and time (self-efficacy score x time) will also be included. Random intercepts will be incorporated for subject specificity in the model to account for clustering effect within subject over time. A hypothesis test for the coefficient of the interaction term (self-efficacy score x time) will be performed to assess the relationship between change on primary outcome (RMBPC reactivity score [2]) and total self-efficacy score [3], over time.

H4: Self-efficacy will partially mediate the relationship between ABC training and burden. In the third step, a mixed effect model on RMBPC reactivity score [2] will be constructed based on the model in H1. We will extend the established model in H1 to include total self-efficacy score as a continuous covariate and the interaction term between total self-efficacy score and time (self-efficacy score x time) will also be included. We expect the interaction term coefficient (group x time) in model for H1 will be significant, and the coefficient of the interaction term between group and time (group x time) will be attenuated and may become non-significant after extending the model to add total self-efficacy score as a covariate and the interaction between total self-efficacy score and time (total self-efficacy score x time). This will indicate that the self-efficacy has a mediated effect on the association between the intervention and change in the primary outcome (RMBPC reactivity score [2]) as compared to the control group. We will also extend these models to include diagnosis, frequency of behavioral symptoms as measured on the RMBPC [2], socio-demographic covariates and preparedness (78). All of results above will be considered significant at $\alpha = 0.05$, with two-sided tests.

Items from the Orbit survey [29] will be examined as repeated weekly measures in each group for an exploratory analysis. We will first explore the data descriptively and then manage or transfer the variables from survey items if needed. Categorical variables will be displayed as frequency (%) and continuous variables will be shown as mean (SD) or median (25^{th} percentile, 75^{th} percentile). These measures will be compared between two groups at each week using two-sample t test for continuous variables and chi-square test for categorical variables. Within each group, we also plan to evaluate the change of measure over time using line charts and compare the line pattern between two groups for continuous variables. The change in continuous variables between two time points within the group can be assessed using paired t-tests. The change in categorical variables between two time points within the group can be assessed using chi-square test.

Aim 3. *Standardize materials and fidelity assessment processes.*
Qualitative data from the focus groups will be analyzed using Thomas's inductive analytic approach [15, 65]. We will create categories that will inform further revision of STELLA-FTD materials to be used in a future NIH Stage 2 study [1].

9) Privacy, Confidentiality and Data Security

Standard institutional practices will be followed as described in the OHSU Information Security and Research Data Resource Guide to maintain the confidentiality and security of data collected in this study. Study staff will be trained with regard to these procedures.

All scales will be de-identified and a participant number will be assigned to each scale for data management. All data will be kept on the limited-access drives or computers at OHSU or in a locked location in the OHSU ADRC. Documents used for the intervention may be stored with the interventionist and RA in a secure location in the staff member's home. All documents will be shredded or returned to the OHSU ADRC at the completion of the intervention. These documents will not contain any PHI, but will contain the participant's study ID #.

Data for this project will be stored in OCTRI's installation of REDCap, a highly secure and robust web-based research data collection and management system.

The REDCap servers are housed behind both the OHSU firewall and a second ACC firewall. All web-based data transmissions are encrypted with industry-standard SSL methods.

Controlled User Access: REDCap is employs a robust multi-level security system that enables researchers to easily implement "minimum necessary" data access for their research staff, including specification of data fields that are identifiers. This feature includes "single click" ability to provide completely deidentified (removing all identified data fields and shifting dates) for analysis or other purposes. User activities are logged to enable auditing of all data access. Access is integrated with OHSU's network such that users who are also OHSU employees are authenticated against their OHSU network credentials.
Data Integrity: REDCap is jointly managed in accordance with OHSU Information Security Directives by ACC staff and members of OCTRI's Biomedical Informatics Program, ensuring fidelity of database configuration and back-ups. User activities are logged to enable auditing of all data changes.

To help us protect subjects' privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers can refuse to disclose information that may identify subjects, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify subjects, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the FDA. A Certificate of Confidentiality does not prevent subjects or members of subjects' families from voluntarily releasing information about them or their involvement in this research. If an insurer, employer, or other person obtains subjects' written consent to receive research information, then the researchers may not use the Certificate to withhold that information. However, if we learn about abuse of a child or elderly person or that a subject intends to harm him or herself or others, or about certain communicable diseases, we will report that to the proper authorities.

Upon enrollment, subjects will be assigned a code that will be used instead of their name, medical record number or other personally identifying information. The video-recordings will show the subjects' faces and the audio will have their voice recordings. Their names and any information discussed during the sessions and focus group will be heard in the audio. The faces, names and audio of any other people who enter the camera/audio zone will also be recorded. We will advise Care Partners that they do not allow anyone (besides themselves) to be in the camera/audio zone during the STELLA-FTD

sessions. However, due to the remote nature of the intervention, we will not have control over who is in the camera/audio zone. On the recordings any information subjects (or anyone else) provides will be identifiable as coming from them and will not be private.

We will provide information to subjects on how to set up a false background for their video sessions so that others who may enter the room have less of a chance of showing up on video.

A key element of STELLA-FTD is to foster peer support. Care Partners will be, asked to share their phone numbers and email addresses with other participants. We will ask all participants to refrain from sharing this information with others outside STELLA-FTD, but we cannot prevent this. The phone numbers and email addresses will not be confidential. We will ask STELLA-FTD participants to only use first names in the intervention.

Encrypted electronic mail will be used for data collection and electronic files will be used for storage of the data and may contain some PHI. Each subject will have a unique ID code. The key associating the codes and the subjects personally identifying information will be restricted to the PI and study staff. The key will be kept secure on a restricted OHSU network drive in a limited access folder. Any paper files will be stored in the restricted-access offices at the Layton Center.

Electronic data will be stored on restricted computers and/or drives on the OHSU network, to which access will require OHSU/ID password authentication.

Video-recordings may be shared with other researchers and those outside of OHSU who are involved in conducting or overseeing research via the secure Webex portal, OneDrive. Using Webex, video streaming links can be sent to identified users via email (which will require a password to access). Study coordinators can download the video files outright from the Webex portal and saved on OHSU's "X" or "H" drives in a highly secure, biometrically authenticated data center or shared via OHSU OneDrive.

Electronic survey data will be stored in a web-accessible server at Qualtrics or REDCap. Copies of this data will be transferred to a secure OHSU server via Application Programming Interface call. Other electronic data will be stored on a secure, password protected OHSU server. Access to data is restricted to study personnel. Access to data requires username/password authentication.

10) Risks and Benefits

a) Risks to Subjects

There are few risks involved in this study. Care Partners will have to meet (via videoconferencing) with the research team and other Care Partners for multiple visits, which may be inconvenient. Care Partners will need to find an activity for their care recipients during the sessions, which may cause financial hardship for some. All visits will be virtual, so there should be no travel costs.

Some of the questions on the scales may seem very personal or embarrassing and fatiguing to participants and may upset them. They may refuse to answer any of the questions that they do not wish to answer. If the questions make them very upset, we will refer them to a social worker.

There is a risk that the video-recordings may be seen by someone they know. It is possible that someone viewing the videos may recognize them, their family members or others and/or hear their names in the audio, and their identities would no longer be confidential. The Care Partners will see each other's' video and audio and share contact information, thus, their identities will not be confidential.

Despite our instruction, care partners will likely text and email us. We cannot control this. We will inform them in consent process of the risks involved.

No part of STELLA-FTD study participation for the Care Partners *should* result in a serious adverse event as defined by the NIA Adverse Event and Serious Adverse Event Guidelines: [66]

> Any adverse event that results in death; is life threatening or places the participant at immediate risk of death from the event as it occurred; requires or prolongs hospitalization; causes persistent or significant disability or incapacity; results in congenital anomalies or birth defects; and/or is another condition which investigators just to represent significant hazard.

There may be other adverse events for Care Partners as defined by the NIA Adverse Event and Serious Adverse Event Guidelines[66]

> Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

Due to the known strain of caregiving, Care Partners may report mental health issues (e.g., anxiety, depression) or physical manifestations of stress (e.g., hypertension, low back pain). These will likely not be related to the intervention, however, emotional distress is a potential risk of study participation, thus training will be provided to all study team members (including all study investigators, Guides and research assistants) to (a) sensitize them to the signs, symptoms and/or indicators of extreme emotional upset, (b) enable them to make an appropriate immediate response and (c) ensure that project protocol, below, for providing information about resources is carried out appropriately.

> Brief Description of the Response Protocol: In the event that any participant displays significant psychological stress as identified by any member of the study team, the Principal Investigator will be notified within 24 hours (Lindauer) (off hours and on weekends, one of the co-PIs or experienced Guides will be notified). Dr. Lindauer (or her delegate) will reach out to the participant with appropriate resources (hotlines, websites, etc.). To the extent possible, these resources will be local to the participant in question. Resources provided to Care Partners are detailed in section 1.3 "Protection Against Study Risks." Dr. Lindauer (or her delegate) will be responsible for reporting adverse events to SO, NIA, IRB during normal reporting intervals.

It is possible that the **persons with FTD** who are enrolled in STELLA-FTD may experience a serious adverse event as defined by the NIA Adverse Event and Serious Adverse Event Guidelines. These SAEs would not be a result of the intervention (the persons with FTD do not participate the intervention). Rather, these events will likely be due to advancing FTD and/or health concerns that come with advancing age (e.g., agitation, falls, urinary tract infections, pneumonia) and are expected. It is expected that some participants with FTD will die, and/or be placed in hospice while they are enrolled in the study.

Hospitalizations and deaths in persons with FTD will be considered expected SAEs for the participants with advancing FTD or conditions associated with aging and therefore reported in quarterly reports

We also expect adverse events for the **persons with FTD** as defined by the NIA Adverse Event and Serious Adverse Event Guidelines.[66] These AEs would not be a result of the intervention (the persons with FTD do not participate the intervention). Rather, these events will likely be due to advancing FTD and/or health concerns that come with advancing age (e.g., agitation, urinary tract infections, pneumonia).

We will report SAEs and AE's per directions laid out by the NIA:

- Only Unexpected SAEs *for those who participate in the intervention* (i.e., only care partners and not the persons with FTD, who are still considered research participants due to measures being collected about them but do not receive the intervention) will be reportable to the IRB, SO and NIA via expedited reporting (i.e., within 48 hours).

- Expedited reporting to NIA PO, SO and IRB (i.e., within 48 hours of study team's awareness) will **only be required for care partners who experience adverse events that are both serious (SAE) and unexpected** (i.e., have not been previously reported for the study's intervention).

- The summary of all other SAEs will be reported to NIA Program Officer and to the Safety Officer **quarterly**, unless otherwise requested by the Safety Officer. SAEs for those who do not participate in the intervention (i.e., persons with FTD) will be reportable quarterly (i.e., in quarterly summary reports).

- Hospitalizations and deaths will be considered expected SAEs for the participants with advancing FTD or conditions associated with aging (i.e., PLWD) and therefore reported in quarterly reports.

a. Potential Benefits to Subjects

Care Partners who complete all training sessions may experience a reduction in their feelings of burden and depression. They may feel less likely to want to place their care recipients in long-term care. It is possible that these benefits will last up to 6 months. In general, they may feel better about caregiving. Care recipients may experience less psychological stress as their Care Partners learn to communicate and manage behaviors.

b) Potential Benefits to Subjects

Care Partners who complete all training sessions may experience a reduction in their feelings of burden It is possible that these benefits will last up to 6 months. In general, they may feel better about caregiving. Care recipients may experience less psychological stress as their Care Partners learn to communicate and manage behaviors.

We will provide a $100 stipend to care partners who complete 4 or more sessions. The stipend will be pro-rated, so care partners who only complete 50% of the active sessions still receive some funds. To facilitate access to STELLA-FTD we will loan care partners laptops and internet access (if needed, see **Technology** below).

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