Title

A randomized controlled trial of emotion regulation therapy for cancer caregivers: A mechanism-targeted approach to addressing caregiver distress

Authors

Applebaum, Allison J
Loschiavo, Morgan
Morgan, Katherine
et al.

Publication Date

2022-11-01

DOI

10.1016/j.cct.2022.106923

Peer reviewed

HHS Public Access

Author manuscript

Contemp Clin Trials. Author manuscript; available in PMC 2022 December 21.

Published in final edited form as:

Contemp Clin Trials. 2022 November ; 122: 106923. doi:10.1016/j.cct.2022.106923.

A randomized controlled trial of emotion regulation therapy for cancer caregivers: A mechanism-targeted approach to addressing caregiver distress

Allison J. Applebaum[a], **Morgan Loschiavo**[a,1], **Katherine Morgan**[b,1], **Douglas S. Mennin**[c], **David M. Fresco**[d], **Michael A. Hoyt**[e], **Elizabeth Schofield**[a], **Mia S. O'Toole**[f], **Julia Cohn**[b], **Jamie M. Jacobs**[b,*]

[a]Memorial Sloan Kettering Cancer Center, NY, New York, United States of America

[b]Massachusetts General Hospital Cancer Center, Boston, MA, United States of America

[c]Teachers College, Columbia University, NY, New York, United States of America

[d]University of Michigan, Ann Arbor, MI, United States of America

[e]University of California- Irvine, Irvine, CA, United States of America

[f]Aarhus University, Denmark

Abstract

Background: Caregivers of patients with cancer play a crucial role in the health of the person they care for, and in the healthcare system at large. Family caregivers receive minimal support, despite being at greater risk for anxiety and depression than patients themselves. Cognitive behavioral therapy (CBT), an effective therapy for anxiety and depression, has shown mixed efficacy when delivered to cancer caregivers. Emotion Regulation Therapy (ERT), a contemporary CBT, may uniquely target processes underlying distress associated with caregiving. Therefore, we adapted both CBT and ERT to target the needs of caregivers (i.e., CBT-C and ERT-C) and are conducting a multi-site randomized trial to examine the comparative efficacy of these interventions.

*Corresponding author at: 55 Fruit Street, Yawkey Center for Outpatient Care, Suite 10B, Boston, MA 02114, United States of America. jjacobs@mgh.harvard.edu (J.M. Jacobs).

[1]Contributed equally as second authors.

CRediT authorship contribution statement

Allison J. Applebaum: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Morgan Loschiavo:** Investigation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Katherine Morgan:** Investigation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Douglas S. Mennin:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration, Funding acquisition. **David M. Fresco:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration. **Michael A. Hoyt:** Conceptualization, Methodology, Investigation, Data curation, Writing – review & editing. **Mia S. O'Toole:** Conceptualization, Methodology. **Julia Cohn:** Project administration, Writing – review & editing. **Jamie M. Jacobs:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

(All co-authors please indicate here if you have any conflicts of interests)

Dr. Applebaum and Dr. Jacobs receive support from Blue Note Therapeutics.

Methods: Family cancer caregivers (n = 200) reporting distress related to caregiving are recruited from two academic cancer centers and randomly assigned to either ERT-C or CBT-C. Caregivers in both interventions engage in eight weekly one-hour sessions by videoconference with a trained interventionist. Caregiver participants complete study assessments at baseline, post-treatment, 3-and 6-months follow-up. Patients of each caregiver can also enroll in the study and complete assessments at baseline and 3-months follow-up. Outcome measures include psychosocial constructs such as anxiety, depression, quality of life, as well as proposed mechanistic constructs and salivary markers of stress and inflammation.

Conclusions: The results of this study will advance the science of caregiving interventions in cancer by addressing a critical gap in our ability to mitigate anxiety and depression in caregivers, as well as further our understanding of how these changes may influence patients' outcomes.

Keywords

Caregivers; cancer; Anxiety; Depression; Psychotherapy; Stress

1. Introduction

Caregivers are partners, relatives, or friends who provide assistance (i.e., physical, emotional) to a patient with often life-threatening, incurable illnesses [1]. In 2016, nearly 5 million people nationwide were caregivers for individuals with cancer [2]. Approximately half of cancer caregivers report clinically significant symptoms of depression and anxiety, with rates higher among caregivers than the patients for whom they provide care [3–5]. Caregiver distress is a result of their capacity to cope with caregiving demands, witness suffering, and live with the possibility of loss. Furthermore, this psychological distress is pervasive across caregivers of patients with varying sites and stages of cancer [6,7]. Distress is associated with psychoneuroimmunological (PNI) changes, such as increased levels of proinflammatory cytokines [14,15] and cortisol [16,17], which are also associated with anxiety and depression, physical illness, stress-related morbidity [18,19], and disturbed sleep [20]. Such distress worsens over time when left untreated [8] and is often associated with downstream medical complications including sleep difficulties, chronic fatigue, cardiovascular disease, increased mortality risk, and poor bereavement outcomes [9–13].

Despite the urgent need for programs that address caregiver distress, a systematic review revealed a lack of empirically supported interventions to target caregiving-related psychological dysfunction [21,27]. Specifically, Cognitive Behavioral Therapy (CBT), which traditionally focuses on perceptions and thoughts as influencers of feelings and behaviors, has been adapted in hopes of better addressing caregiver distress [23,25]. CBTs enriched with mindfulness offer comparatively greater efficacy than standard CBT. There may be an opportunity to ensure that traditional CBT or burden-focused psychoeducational approaches more comprehensively address caregiver distress. For example, conceptualization of distress in caregivers may need to incorporate worry and rumination, as caregivers often become caught in perseverative negative thinking (PNT; e.g., rumination, self-criticism) [28,29]. Traditional CBT may be limited in targeting both earlier and later components of the distressing emotional cascade [30]. Seeking to more

comprehensively target worry and rumination, we developed a reformulated CBT, Emotion Regulation Therapy for Cancer Caregivers (ERT-C), that systematically addresses multiple components of the distress context.

ERT, the intervention from which ERT-C was adapted, is a theoretically derived, mechanism focused treatment that integrates findings from affect science with CBT principles to target and normalize neuro-behavioral deficits underlying worry and rumination by increasing motivational awareness and improving attentional and metacognitive regulation capacities [31,32]. For instance, findings indicate that ERT demonstrates clinical efficacy in distress disorders (e.g., generalized anxiety disorder, major depressive disorder) [32–35,40] by promoting flexible and sustained attention as well as metacognitive capacities such as decentering (i.e., observing thoughts that arise in the mind with distance and perspective) and reappraisal (i.e., reinterpreting the meaning of an event to change its emotional trajectory) (Hedges' g's = 0.6 to 2.6) [32,34,36,37,55]. Further, ERT-linked neural changes in resting state connectivity, were associated with decreases in clinical severity (r's = 0.4–0.6) and increases in flexible attention (r's = 0.3–0.5) [38] gains in decentering and reductions in worry [39].

ERT has since been adapted for cancer caregivers (ERT-C). An open trial evaluating ERT-C's efficacy in caregivers indicated statistically significant reductions in worry, rumination, anxiety, and depression symptoms after 8 sessions, which were largely maintained through a 6-month follow-up [40]. Notably, although caregiver distress often negatively impacts cancer patients' functioning and well-being [42,43], our pilot RCT with 81 caregivers of patients with various sites and stages of cancer revealed that the identified cancer patients of caregivers receiving ERT-C also experienced a large increase in quality of life (QOL) compared to patients whose caregivers were in a waitlist condition (Hedge's g = 0.90). Our recent work suggests that ERT-C confers clinical benefit via increases in attentional and metacognitive regulatory ability [33,35,41].

Furthermore, participation in ERT-C or CBT-C may lead to reductions in biomarkers of stress and systemic inflammation in caregivers. For example, we demonstrated an ERT-C linked reduction in proinflammatory markers ranging from 2% to 33% in a subset of caregivers (N = 15). In our recent randomized controlled trial, caregivers receiving ERT-C evidenced a non-significant but notable decrease in proinflammatory cytokine Interluekin-6 (IL-6) as compared to patients in the waitlist control arm (g = 0.36) [44]. As such, ERT-C may ameliorate physiological correlates of distress in caregivers, with significant downstream effects on their overall health and well-being.

The purpose of the present study is to rigorously evaluate the efficacy of ERT-C, compared to CBT adapted for caregivers (CBT-C), and elucidate potential mechanisms underlying reductions in distress through a randomized, controlled, repeated measures design.

1.1. Study aims

Aim 1 will compare the immediate and longer-term efficacy of ERT-C versus CBT-C in improving symptoms of anxiety, depression, rumination and worry. This study will compare ERT-C and CBT-C on improvements in caregiver primary (i.e., anxiety and depression,

worry, rumination) and secondary (i.e., QOL and burden) outcomes and whether these gains are maintained at 6-months follow-up. Additionally, we will examine whether ERT-C or CBT-C will lead to greater improvements in patient outcomes at 3-months follow-up. As an exploratory hypothesis, we will also assess putative moderators (including cancer site, stage, and caregivers' sociodemographic factors) of the efficacy of ERT-C versus CBT-C.

Aim 2 will assess the indirect effects of attention and metacognitive regulation on primary and secondary caregiver outcomes and whether these effects will be more pronounced in ERT-C or CBT-C. We hypothesize that only skills that specifically target components of distress (i.e., attention regulation, metacognitive regulation) will mediate primary and secondary caregiver outcomes compared to other facets of improving the caregiving experience (i.e., reducing perceived burden, maladaptive behavioral coping), and that gains and mediation in attention and metacognitive regulation will be more pronounced in ICs receiving ERT-C than CBT-C.

Lastly, Aim 3 will evaluate differential effects of treatment on change in biomarkers overall and by treatment arm. We will examine whether ERT-C or CBT-C will result in greater reductions in cortisol dysregulation and systemic inflammation, and whether gains will be maintained at a 6-month follow-up. Further, our exploratory hypothesis will examine whether reductions in cortisol dysregulation and systemic inflammation observed with ERT-C or CBT-C will be most prominent in caregivers with baseline elevations in distress.

2. Materials and methods

This study is a multi-site trial including recruitment from two sites, Memorial Sloan Kettering Cancer Center (MSK, IRB #20–407) and Massachusetts General Hospital (MGH, IRB #21–074) Cancer Center (ClinicalTrials.gov Identifier NCT04802720). The study was approved by the MSK Institutional Review Board, the IRB of record, and subsequently the Dana Farber/Harvard Cancer Center IRB (DF/HCC). Recruitment procedures comply with HIPAA guidelines.

2.1. Study design

This study follows the design shown in Fig. 1. Distressed caregivers of patients with any site or stage of cancer who are currently receiving cancer treatment of any kind (e.g., curative, palliative) at MSK (n = 100) or MGH (n = 100) are eligible for participation. We also offer enrollment to the patients (n = 200) they are caring for, though caregiver participation is not contingent on patient participation. At MSK, study staff screen interested caregivers who respond to digital fliers posted on the MSK caregiver website (https://www.mskcc.org/experience/caregivers-support) via telephone for eligibility. Caregivers on the waitlist for the MSK Caregivers Clinic are also assessed for interest and screened for eligibility over the phone by study staff. At MGH, study staff screen clinic schedules to identify patients who may have eligible caregivers and contact those patients (with permission from their oncology clinician) to reach their caregivers, as well as post study flyers and accept referrals from social work, psychology, and psychiatry. Interested and eligible caregivers provide informed consent and enroll in the study. Caregiver participants are registered and randomized 1:1 to ERT-C or CBT-C and complete baseline assessments (T1) of self-reported outcomes

and saliva samples to assess inflammatory markers and cortisol levels. Caregivers meet with study therapists for 8 one-on-one weekly sessions of either ERT-C or CBT-C via videoconference. Each session is 60 min in length and is audio- or video-recorded. Caregiver participants repeat assessments at post-intervention (T2), 3 months post-intervention (T3), and 6 months post-intervention (T4); caregivers also complete assessments mid-intervention at weekly therapeutic sessions to assess mechanistic measures and outcomes of depression and anxiety. Patient participants complete patient-reported survey assessments at baseline (T1) and 3 months post-intervention (T3) (Table 1). If the patient dies while the caregiver is participating in the intervention, the caregiver can still continue with the study and receives abbreviated follow-up assessments that exclude caregiving-specific measures. Study data are collected and managed using REDCap electronic data capture tools hosted through MSK.

2.2. Participant eligibility criteria

To be eligible, caregivers must report that they experience distress as evidenced by a score of 4 or greater on the Distress Thermometer [46] and report that their distress is related to their caregiving experience or that their distress started/has gotten worse since the patient was diagnosed/began treatment. In addition, caregivers must be ≥18 years of age, be caring for a patient receiving any type of care (e.g., curative, palliative) at MSK or MGH in the past 12 months, be English-fluent, reside in New York/New Jersey (MSK) or Massachusetts (MGH), and have no severe cognitive impairments, history of severe mental illness, or medical condition known to confound measures of systemic inflammation or interfere with study participation. Caregivers who are already engaged in psychotherapy are eligible if they are able and willing to put that therapy on hold for the course of treatment.

Eligible patients are ≥18 years of age, receiving care from an enrolled caregiver participant, English-speaking, and have no severe mental illness and/or cognitive impairment.

2.3. Intervention

CBT-C and ERT-C treatments are each 8-session, individual, caregiver-directed interventions delivered by a trained study therapist and facilitated by a manualized workbook with between-session practice exercises. Participants in both conditions have access to an online website that houses study materials as well as intervention-specific audio-recorded relaxation and meditation exercises. To accommodate caregivers and to maximize attendance, the 8 sessions are to be completed within 8 to 16 weeks from initiation of the first session. Each session is 60 min long and conducted through the telehealth platform approved by each site's Privacy Board (WebEx for MSK, Zoom for MGH).

2.3.1. CBT-C—Cognitive Behavioral Therapy (CBT) is an evidence-based psychotherapeutic approach grounded in the cognitive model that a person's emotional, behavioral, and physiological reactions to a situation is based on their appraisal of that situation [47]. CBT adapted for cancer caregivers, Cognitive Behavioral Therapy for Cancer Caregivers (CBT-C), aims to ameliorate caregivers' distress levels by challenging and changing unhelpful cognitions and behaviors and improving personal coping strategies. CBT-C modules incorporate information specific to the caregiving context throughout and train caregivers in: 1) problem-focused and emotion-focused coping based on the

controllability of the stressor (i.e., coping effectiveness training), 2) cognitive restructuring to adjust and reframe automatic thought distortions, 3) skills such as behavioral activation and time-based activity pacing to maximize engagement in daily routines and optimize self-care, 4) relaxation training as a tool to cope with stress by engaging the relaxation response. Modules incorporate skills for relaxation and information specific to the caregiving context throughout. The sessions are outlined in Fig. 2.

2.3.2. ERT-C—Emotion Regulation Therapy for Cancer Caregivers (ERT-C) is an 8-session intervention built on foundations of CBT to address motivational processing components of the caregiving context while targeting attentional and metacognitive components of worry and rumination and resultant maladaptive behavioral coping. ERT-C utilizes modules consisting of: 1) self-monitoring of problematic motivational (i.e., threat and/or loss-based) and dysregulatory (i.e., worry, rumination, self-criticism, reassurance seeking, avoidance/withdrawal, and/or compulsive behaviors) responses within evocative and burdensome caregiving contexts; 2) attention regulation skills to increase the ability to broaden, shift, and sustain attention when distressed; 3) metacognitive regulation skills (e.g., decentering and reappraisal) to more effectively distance and reframe emotional thoughts; and 4) adaptive engagement in contexts that are intrinsically rewarding even when accompanied by loss/threat via contextual application of learned skills [32,37]. The particular skills introduced in ERT-C are supported by brief mindfulness meditation practices. Session content is outlined in Fig. 2.

2.3.3. Intervention training, supervision, and integrity—Study therapists are predoctoral psychology fellows and licensed psychologists who undergo comprehensive training in either CBT-C or ERT-C. Supervision is led by the investigative team via videoconference on a weekly basis for all study therapists in ERT-C (DM, DF), and CBT-C (AA, JJ), separately. All sessions are video-recorded and a random sample of 30% of cases (100% of videotaped sessions for these participants) are evaluated and rated for treatment integrity. An independent licensed clinical psychologist with considerable experience conducting ERT-C or CBT-C provides treatment integrity ratings for their respective treatment arm using comprehensive treatment and coding manuals. Raters offer written feedback to individual facilitators regarding the specific individual session to enhance continued training and supervision in these individual interventions. Raters are not blinded to the therapist, the intervention arm, or the specific session within that treatment arm and are required to achieve >80% inter-rater reliability. Feedback on recorded sessions is also incorporated into supervision sessions.

2.4. Outcomes

2.4.1. Participant characteristics—Participant characteristics are collected at baseline through the Demographic Information and Psychosocial Services Use, Preferences, and Perceived Barriers survey. This measure, adapted from a prior study [77], uses Likert-scale ratings and open-ended questions to gather self-reported data on demographic information, past/current psychosocial service use, support needs, intervention preferences, and perceived barriers.

2.4.2. Outcomes—See Table 1 for all outcomes and time points.

2.4.3. Measures

2.4.3.1. Distress.: The Distress Thermometer is a single-item visual analog scale widely used to screen patients with cancer and ICs for distress with a 0–10 range accompanied by a 34-item problem checklist [46,48,49,50]. A score of 4 or greater indicates clinically significant distress.

2.4.3.2. Anxiety and depression.: Hospital Anxiety and Depression Scale (HADS) is a 14-item questionnaire of overall psychological distress, well-tested in cancer populations [51,52]. A higher score indicates higher distress.

2.4.3.3. Worry.: Penn State Worry Questionnaire is a widely-used measure of future oriented trait worry consisting of 16-items, with higher scores indicate greater worry. [53,54]

2.4.3.4. Rumination.: Rumination-Reflection Questionnaire, Rumination subscale (RRQ-R) is 12-item measure of perseverative thinking about the past and loss [55]. Higher scores indication greater rumination.

2.4.3.5. Attentional ability.: Attentional Control Scale (ACS) is a 20-item measure of the capacity to control attention in relation to positive and negative reactions, for which subscales assess attentional focus and shifting ability [56]. Higher scores indicate better attentional abilities.

2.4.3.6. Decentering.: Experiences Questionnaire, Decentering subscale (EQ-D) is an 11-item measure of disidentification with content of negative thinking [32]. Higher scores indicate better disidentification skills.

2.4.3.7. Emotion regulation capacity.: Emotion Regulation Questionnaire, Reappraisal subscale (ERQ-R) is a 6-item measure of cognitive reappraisal, the ability to adopt a different cognitive perspective on a current situation [57]. Higher scores indicate better emotion regulation abilities.

2.4.3.8. Quality of life.: Caregiver Quality of Life Index-Cancer is a 35-item measure assessing the physical, emotional, social, and financial QOL of caregivers [65].

2.4.3.9. Caregiver burden.: Caregiver Reaction Assessment measures several dimensions of caregiver burden including self-esteem, family support, finances, and health. It has been widely used in caregiver studies [65,66].

2.4.3.10. Comorbid medical problems.: Self-Administered Comorbidity Questionnaire is a 15-item scale assessing 12 defined medical problems and 3 optional conditions. Higher scores indicate greater medical severity [67].

2.4.3.11. Global mental and physical health.: Patient-Reported Outcomes Measurement Information System – Global Health Scale is an item bank developed by the NIH to assess mental and physical health [68,69].

2.4.3.12. Expectation of treatment outcome.: Credibility and Expectancy Questionnaire is a 6-item measure of participants' reactions to treatments, including ratings of acceptability and belief about treatment effectiveness [71,72]. This measure has been adapted to cancer caregivers. It has been widely-used in prior research and has demonstrated strong psychometric properties [72].

2.4.3.13. Cancer patient quality of life.: EORTC QLQ-C30 is a 30-item questionnaire specifically developed to measure QOL in cancer patients [73].

2.4.3.14. Perceived stress.: Perceived Stress Scale is a widely-used 9-item measure of the degree to which situations are perceived as stressful. It has demonstrated adequate validity and reliability [74,75].

2.4.3.15. Healthcare service utilization.: The National Survey on Drug Use and Health contains 5 questions asking about the frequency and nature of health service utilization in the past 12 months [76].

2.4.3.16. Biological markers of stress and inflammation.: We will assess biomarkers IL-6, CRP, and sTNFαRII indicative of systemic inflammation and are associated with distress. Pro-inflammatory cytokine levels are assessed via oral mucosal transudate (OMT), an ultrafiltrate of blood and a reflection of serum, rather than saliva. sTNFαRII collected via OMT has been validated in HIV-infected patients [58]. Like markers of systemic inflammation, oral inflammatory activity increases in response to social stress and depression suggesting a relation between systemic and oral inflammatory activity [59–61]. OMT is collected using the OraSure collection device [62]. Upon return, samples are centrifuged at 800*g* for 15 min to elute the sample. The eluate is transferred into a 4 ml cryovial and frozen at −80 °C until assay. Cytokine levels is determined by immunosorbent assay (ELISA) according to assay manufacturer's protocols. Sample processing, storage, and analysis takes place at the Interdisciplinary Institute for Salivary Bioscience Research (IISBR) at the University of California, Irvine. All samples are run in duplicate, and assays are repeated on two separate days; intra-assay and inter-assay mean levels will be used in all analyses.

Furthermore, diurnal rhythm in salivary cortisol is measured over three days at each major timepoint. Caregivers collect saliva samples upon awakening, 30 min later, 8 h later, and at bedtime [63]; they are instructed to go about their normal daily activities on data collection days and complete a diary to assess relevant health behaviors (e.g., caffeine, tobacco, and alcohol consumption; physical activity, sleep) and daily stress. To avoid sample contamination, caregivers are instructed to avoid brushing their teeth, eating, or drinking within 20 min presampling and to keep samples frozen prior to returning them to the research laboratory. Returned salivettes are stored in a – 20-degree Celsius freezer until analysis. After data collection is complete, salivary cortisol is analyzed with a time-resolved

fluorescence immunoassay at the IISBR laboratory. Several indices are computed including diurnal slope, area under the daily curve, cortisol awakening response, and total daily cortisol output.

2.5. Statistical analyses

The primary analytic approach to testing treatment efficacy in Aim 1 and change in biomarkers in Aim 3 will be Generalized Linear Mixed-Effects Model (GLIMMIX191), also known as Hierarchical Linear Model (HLM192). For Aim 2, we will utilize parallel process latent growth curve modeling (PP-LGCM), which is similar to a combination of growth curve models with the Baron and Kenny approach, to test mediation of ERT-C on anxiety and depression via emotion regulation skills. PP-LGCM allows tests of both direct and indirect effects of treatment on outcomes through hypothesized pathways.

2.5.1. Aim 1—We will test differential effects of ERT-C versus CBT-C using separate Generalized Linear Mixed-Effects Models for each outcome (e.g., depression, anxiety). Each model will include random effects for both site and caregiver. These random, per-caregiver intercepts will account for individual variation among caregivers, while still allowing a test of the fixed effects (i.e., treatment group). This flexible analytic strategy will also allow testing of non-linear time effects, treatment differences immediately post-treatment, and comparison of 6-month maintenance, all within the same model framework via specific contrasts. For immediate gains, data will be restricted to T1 to T2 (including the mid-intervention assessments for HADS outcomes). For 6-month maintenance, a similar model will be estimated, restricted to the post-intervention data. For HADS outcomes pre- to postintervention, 10 assessments (T1, T2, and 8 mid-intervention timepoints) are expected; for all 4 primary outcomes, 3 timepoint assessments (T2, T3, T4) are expected for 6-month maintenance. Superiority is defined by a significant finding on post-treatment difference (T1 to T2) and either further significant differentiation post-intervention (T3 to T5) or no statistically significant differentiation if the CBT-C group converges with the ERT-C group during this time.

2.5.2. Aim 2—We will assess gains in emotion regulation as well as reductions in anxiety and depressive symptoms via growth curve modeling. First, for both emotion regulation skills and outcomes, a series of traditional growth curve models will assess the effect of ERT-C (versus CBT-C) on each potential mediator from the ACS, EQ-D, ERQ-R, and COPE instruments which are assessed weekly during the intervention. Next, for each outcome, similar growth curve models will be used to assess the overall effect (direct and indirect) of ERT-C on outcomes both during the intervention and at major timepoints. We will employ parallel process latent growth curve modeling to assess the mediational process provided by weekly data. This analysis will be conducted using M-Plus software.

2.5.3. Aim 3—The same HLM/GLIMMIX framework from Aim 1 will be used for Aim 3. The analysis will be similarly conducted to assess both differential pre-post change (T1 to T2) and maintenance at 6-months follow-up (T2 to T4), using appropriate contrasts on the time variable. This same framework will allow for testing the exploratory moderation hypothesis. Specifically, outcomes will be regressed on the ERT-C indicator, an indicator

of elevated baseline distress, and the interaction of the two. A significant finding on the interaction term will be evidence to a moderation effect and will be followed with stratified analyses of the biomarker outcomes by baseline distress category and treatment arm.

2.6. Sample size and power

Findings from prior ERT-C trials indicate a pre-treatment to posttreatment effect size of $g = 0.49$ on depression and anxiety [44,70]. A recent meta-analysis found very small ($g = 0.08$) effects of CBT on these outcomes–suggesting a differential effect size of Cohen's $d = 0.41$. Using an HLM model with up to 3 time points, a within-subject ICC of 0.2, allowing for approximately 20% attrition, and setting Type I error to the conservative value of 0.0125 to account for 4 primary outcomes, we simulate 90.4% power for the differential pre-treatment to post-treatment changes for Aim 1 if the effect size is at least $g = 0.41$ and 82.8% power for a more conservative effect of $g = 0.37$. Power was simulated using the simr package in R. For patient outcomes, the PI anticipates at least 50% enrollment of patients associated with the caregivers, and comparable attrition between patients and caregivers. Enrollment of 100 patients, with 80% retention at the 3-month follow-up assessment will provide 80% power to detect a standardized effect of at least $d = 0.63$ for the difference in change scores using an independent samples t-test approximation at alpha of 0.05. Similarly, for rumination and worry from pre to post intervention, enrollment of 200 ICs with 10% attrition during intervention will provide 80% power to detect a medium effect of at least $d = 0.50$ with alpha of 0.0125.

Statistical power for mediation models was estimated from simulations by Fritz and MacKinnon, which provide conservative estimates given the reduction in noise provided by our weekly assessments and growth curve modeling. Allowing for up to 20% attrition, the sample will provide at least 80% power to detect mediation using the Sobel test if one of the two paths (α or β) has a small-medium effect size ($d = 0.39$), and the other has at least a small effect ($d = 0.26$).

Based on previous participation rates with biological samples at our institutions, we anticipate at least 75% of the 200 enrolled caregivers to provide samples. With a conservative 20% attrition assumption, an analytic sample of $n = 120$ will provide 80% power to detect a small-medium effect size of $d = 0.36$ for the t-test for Hypothesis 3a.

3. Discussion

The unmet needs of cancer caregivers were clear long before the COVID-19 pandemic, but our current challenges have amplified the role of caregivers as the backbone of the healthcare system in the United States. Caregivers require education and support to fulfill their critical roles and responsibilities. The current investigation represents one of the first trials to examine the comparative efficacy and potential mechanisms of two active psychotherapies developed specifically to address the unique needs of cancer caregivers, to assess the impact of such intervention on PNI outcomes among caregivers, and to evaluate the downstream effects of caregiver outcomes on patient QOL. We acknowledge that this trial has certain limitations, including that we have not tested CBT-C in prior studies and therefore cannot exact an anticipated effect size as we are able to do with

ERT-C. To further understand the comparative effects of CBT-C and ERT-C, we will investigate whether the interventions target discrete mechanisms by exploring the impact of gains in adaptive emotion regulation skills in improving caregiver outcomes, and whether these gains are variable across arms. For example, attention regulation and metagcognitive regulation may be more pronounced in caregivers randomly assigned to ERT-C, while behavioral coping and reductions in perceived burden may be more pronounced in caregivers randomly assigned to CBT-C. In addition, while we considered cross-training therapists to ensure equivalency in delivery of the study interventions, we opted not to in an effort to minimize cross-contamination of intervention components. Instead, we have ensured equity across CBT-C and ERT-C by 1) monitoring years of clinical experience of therapists assigned to each arm to ensure equivalent skill level; 2) requiring equivalent training for both interventions (i.e., interventionists on both study arms participate in a half-day virtual training, read relevant materials and familiarize themselves with the study manual, engage in procedural training with staff coordinators, practice and role play delivery of intervention techniques, listen to prior audio and/or video-recorded sessions, attend and participate in weekly supervision to discuss ongoing cases, and undergo audio and/or video review of their current cases on a weekly basis); and 3) providing equivalent supervision from two trained experts in a Co-PI and Co-I study pair (AA and JJ on CBT-C, and DM and DF on ERT-C). Furthermore, while we are not mandating patient participation in this study in order to maximize heterogeneity in our caregiver sample, we acknowledge that this may lead to some homogeneity in our patient sample (e.g., patients with more advanced disease may be less likely to participate). Strengths of the study include the brevity of both interventions and virtual delivery modality that maximizes participation, especially considering the time constraints of caregivers who are already overwhelmed with daily responsibilities. In the long term, this study will elucidate a most efficacious intervention for caregivers and lead to a greater understanding of how to improve caregiver outcomes, as well as patient outcomes that may be downstream of caregiver improvements. Our hope is that this work will result in refined efficacious interventions that can assist caregivers in capitalizing on the challenges of their caregiving journeys as opportunities to develop resilience and strength, and that this can buffer the significant and negative psychological and PNI effects of caregiving.

Acknowledgements

The authors would like to acknowledge the family members and patients who have or are participating in this study. In addition, the authors would like to extend their appreciation to the study therapists who have dedicated their time to training and delivering these interventions as part of this study.

Funding

This work was supported by the National Institutes of Health (R01CA244185, P30CA008748).

Data availability

No data was used for the research described in the article.

References

[1]. National Alliance for Caregiving, Caregiving in the U.S. 2009. AARP Research Data, 2009, 10.26419/res.00062.008.

[2]. National Alliance for Caregiving in Collaboration with AARP, Cancer caregiving in the U.S.: an intense, episodic, and challenging care experience. Research Report, 2016.

[3]. Braun M, Mikulincer M, Rydall A, Walsh A, Rodin G, Hidden morbidity in cancer: spouse caregivers, J. Clin. Oncol 25 (30) (2007) 4829–4834, 10.1200/jco.2006.10.0909. [PubMed: 17947732]

[4]. Kim Y, Shaffer KM, Carver CS, Cannady RS, Prevalence and predictors of depressive symptoms among cancer caregivers 5 years after the relative's cancer diagnosis, J. Consult. Clin. Psychol 82 (1) (2014) 1–8, 10.1037/a0035116. [PubMed: 24364792]

[5]. Askari A, Madgaonkar S, Rowell R, Current psycho-pathological issues among partners of cancer patients, J. Psychos. Res 7 (1) (2012) 77.

[6]. Proot IM, Abu-Saad HH, Crebolder HF, Goldsteen M, Luker KA, Widdershoven GA, Vulnerability of family caregivers in terminal palliative care at home; balancing between burden and capacity, Scand. J. Caring Sci 17 (2) (2003) 113–121, 10.1046/j.1471-6712.2003.00220.x. [PubMed: 12753511]

[7]. Mehta A, Chan LS, Cohen SR, Flying blind: sources of distress for family caregivers of palliative cancer patients managing pain at home, J. Psychosoc. Oncol 32 (1) (2014) 94–111, 10.1080/07347332.2013.856057. [PubMed: 24428253]

[8]. Lambert SD, Jones BL, Girgis A, Lecathelinais C, Distressed partners and caregivers do not recover easily: adjustment trajectories among partners and caregivers of cancer survivors, Ann. Behav. Med 44 (2) (2012) 225–235, 10.1007/s12160-012-9385-2. [PubMed: 22740365]

[9]. Carter PA, Family caregivers' sleep loss and depression over time, Cancer Nurs. 26 (4) (2003) 253–259, 10.1097/00002820-200308000-00001. [PubMed: 12886115]

[10]. Cho MH, Dodd MJ, Lee KA, Padilla G, Slaughter R, Self-reported sleep quality in family caregivers of gastric cancer patients who are receiving chemotherapy in Korea, J. Cancer Educ 21 (1, suppl) (2006) S37–S41, 10.1207/s15430154jce2101s_8. [PubMed: 17020500]

[11]. Buyck J, Ankri J, Dugravot A, Bonnaud S, Nabi H, Kivimaki M, Singh-Manoux A, Informal caregiving and the risk for coronary heart disease: the Whitehall II study, J. Gerontol. Ser. A Biol. Med. Sci 68 (10) (2013) 1316–1323, 10.1093/gerona/glt025.

[12]. Tiukinhoy S, Rochester CL, Mortality after the hospitalization of a spouse, J. Cardpulm. Rehabil 26 (3) (2006) 192, 10.1097/00008483-200605000-00016.

[13]. Koop P, Strang V, Predictors of bereavement outcomes in families of patients with cancer: a literature review, Can. J. Nurs. Res 29 (4) (1997) 33–50. https://cjnr.archive.mcgill.ca/article/download/1409/1409/0. [PubMed: 9697434]

[14]. Bass DM, Judge KS, Snow AL, Wilson NL, Looman WJ, McCarthy C, Morgan R, Ablorh-Odjidja C, Kunik ME, Negative caregiving effects among caregivers of veterans with dementia, Am. J. Geriatr. Psychiatry 20 (3) (2012) 239–247, 10.1097/jgp.0b013e31824108ca. [PubMed: 22251867]

[15]. Vitaliano PP, Murphy M, Young HM, Echeverria D, Borson S, Does caring for a spouse with dementia promote cognitive decline? A hypothesis and proposed mechanisms, J. Am. Geriatr. Soc 59 (5) (2011) 900–908, 10.1111/j.1532-5415.2011.03368.x. [PubMed: 21568959]

[16]. Cohen M, Klein E, Kuten A, Fried G, Zinder O, Pollack S, Increased emotional distress in daughters of breast cancer patients is associated with decreased natural cytotoxic activity, elevated levels of stress hormones and decreased secretion of Th1 cytokines, Int. J. Cancer 100 (3) (2002) 347–354, 10.1002/ijc.10488. [PubMed: 12115552]

[17]. Miller GE, Chen E, Sze J, Marin T, Arevalo JM, Doll R, Ma R, Cole SW, A functional genomic fingerprint of chronic stress in humans: blunted glucocorticoid and increased NF-κb signaling, Biol. Psychiatry 64 (4) (2008) 266–272, 10.1016/j.biopsych.2008.03.017. [PubMed: 18440494]

[18]. Lengacher CA, Kip KE, Barta M, Post-White J, Jacobsen PB, Groer M, Lehman B, Moscoso MS, Kadel R, Le N, Loftus L, Stevens CA, Malafa MP, Shelton MM, A pilot study evaluating the effect of mindfulness-based stress reduction on psychological status, physical status, salivary cortisol, and interleukin-6 among advanced-stage cancer patients and their caregivers, J. Holist. Nurs 30 (3) (2012) 170–185, 10.1177/0898010111435949. [PubMed: 22442202]

[19]. Miller GE, Cohen S, Ritchey AK, Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid-resistance model, Health Psychol. 21 (6) (2002) 531–541, 10.1037/0278-6133.21.6.531. [PubMed: 12433005]

[20]. Potier F, Degryse J, De Saint-Hubert M, Impact of caregiving for older people and pro-inflammatory biomarkers among caregivers: a systematic review, Aging Clin. Exp. Res 30 (2) (2017) 119–132, 10.1007/s40520-017-0765-0. [PubMed: 28474314]

[21]. Applebaum AJ, Breitbart W, Care for the cancer caregiver: a systematic review, Palliative Support. Care 11 (3) (2012) 231–252, 10.1017/s1478951512000594.

[23]. Beck JS, Cognitive Therapy: Basics and beyond, Guilford Press, 1995.

[25]. Scott JL, Dawkins S, Quinn MG, Sanderson K, Elliott KJ, Stirling C, Schüz B, Robinson A, Caring for the carer: a systematic review of pure technology-based cognitive behavioral therapy (TB-CBT) interventions for dementia carers, Aging Ment. Health 20 (8) (2015) 793–803, 10.1080/13607863.2015.1040724. [PubMed: 25978672]

[27]. O'Toole MS, Zachariae R, Renna ME, Mennin DS, A. Applebaum, Cognitive behavioral therapies for informal caregivers of patients with cancer and cancer survivors: a systematic review and meta-analysis, Psycho-Oncology 26 (4) (2016) 428–437, 10.1002/pon.4144. [PubMed: 27147198]

[28]. Mennin DS, Fresco DM, Emotion regulation therapy, in: Gross JJ (Ed.), Handbook of Emotion Regulation, 2nd ed, Guilford Press, 2013, pp. 469–490.

[29]. Kolubinski DC, Nikčević AV, Lawrence JA, Spada MM, Metacognitions about self-critical rumination questionnaire, PsycTESTS Dataset. (2017), 10.1037/t64534-000.

[30]. Fresco DM, Mennin DS, All together now: utilizing common functional change principles to unify cognitive behavioral and mindfulness-based therapies, Curr. Opin. Psychol 28 (2019) 65–70, 10.1016/j.copsyc.2018.10.014. [PubMed: 30502664]

[31]. Mennin DS, Fresco DM, What, me worry and ruminate about DSM-5 and RDoC? The importance of targeting negative self-referential processing, Clin. Psychol. Sci. Pract 20 (3) (2013) 258–267, 10.1111/cpsp.12038.

[32]. Fresco DM, Moore MT, Van Dulmen MH, Segal ZV, Ma SH, Teasdale JD, Williams JM, Initial psychometric properties of the experiences questionnaire: validation of a self-report measure of decentering, Behav. Ther 38 (3) (2007) 234–246, 10.1016/j.beth.2006.08.003. [PubMed: 17697849]

[33]. Mennin DS, Fresco DM, Ritter M, Heimberg RG, An open trial of emotion regulation therapy for generalized anxiety disorder and cooccurring depression, Depress. Anxiety 32 (8) (2015) 614–623, 10.1002/da.22377. [PubMed: 25945946]

[34]. Renna ME, Quintero JM, Soffer A, Pino M, Ader L, Fresco DM, Mennin DS, A pilot study of emotion regulation therapy for generalized anxiety and depression: findings from a diverse sample of young adults, Behav. Ther 49 (3) (2018) 403–418, 10.1016/j.beth.2017.09.001. [PubMed: 29704969]

[35]. Mennin DS, Fresco DM, O'Toole MS, Heimberg RG, A randomized controlled trial of emotion regulation therapy for generalized anxiety disorder with and without co-occurring depression, J. Consult. Clin. Psychol 86 (3) (2018) 268, 10.1037/ccp0000289. [PubMed: 29504794]

[36]. Mennin DS, Fresco DM, Ritter M, Heimberg RG, An open trial of emotion regulation therapy for generalized anxiety disorder and comorbid depression, Depress. Anxiety 32 (8) (2015) 614–623. [PubMed: 25945946]

[37]. Ochsner KN, Gross JJ, The cognitive control of emotion, Trends Cogn. Sci 9 (5) (2005) 242–249. [PubMed: 15866151]

[38]. Scult MA, et al. , Changes in functional connectivity following treatment with emotion regulation, Therapy. 13 (2019).

[39]. Fresco DM, et al. ., Distinct functional connectivities predict clinical response with emotion regulation therapy, Front. Hum. Neurosci 11 (2017) 86. [PubMed: 28316567]

[40]. Applebaum AJ, Panjwani AA, Buda K, O'Toole MS, Hoyt MA, Garcia A, Fresco DM, Mennin DS, Emotion regulation therapy for cancer caregivers—an open trial of a mechanism-targeted approach to addressing caregiver distress, Transl. Behav. Med 10 (2) (2018) 413–422, 10.1093/tbm/iby104.

[41]. O'Toole MS, Renna ME, Mennin DS, Fresco DM, Changes in decentering and reappraisal temporally precede symptom reduction during emotion regulation therapy for generalized anxiety disorder with and without co-occurring depression, Behav. Ther 50 (6) (2019) 1042–1052, 10.1016/j.beth.2018.12.005. [PubMed: 31735240]

[42]. Langer SL, Brown JD, Syrjala KL, Intrapersonal and interpersonal consequences of protective buffering among cancer patients and caregivers, Cancer 115 (S18) (2009) 4311–4325, 10.1002/cncr.24586. [PubMed: 19731352]

[43]. Li Q, Loke AY, A literature review on the mutual impact of the spousal caregiver–cancer patients dyads: 'communication', 'reciprocal influence', and 'caregiver–patient congruence', Eur. J. Oncol. Nurs 18 (1) (2014) 58–65, 10.1016/j.ejon.2013.09.003. [PubMed: 24100089]

[44]. O'Toole MS, Mennin DS, Applebaum A, Weber B, Rose H, Fresco DM, Zachariae R, A randomized controlled trial of emotion regulation therapy for psychologically distressed caregivers of cancer patients, JNCI Cancer Spect. 4 (1) (2019), 10.1093/jncics/pkz074.

[46]. Roth AJ, Kornblith AB, Batel-Copel L, Peabody E, Scher HI, Holland JC, Rapid screening for psychologic distress in men with prostate carcinoma, Cancer 82 (10) (1998) 1904–1908, 10.1002/(sici)1097-0142(19980515)82:10<1904::aid-cncr13>3.0.co;2-x. [PubMed: 9587123]

[47]. Beck JS, Cognitive Behavior Therapy: Basics and beyond, 3rd ed., Guilford Publications, 2020.

[48]. Liu F, Huang J, Zhang L, Fan F, Chen J, Xia K, Liu Z, Screening for distress in patients with primary brain tumor using distress thermometer: a systematic review and meta-analysis, BMC Cancer 18 (1) (2018), 10.1186/s12885-018-3990-9.

[49]. Ownby K, ACHPN, AOCN, K, Use of the distress thermometer in clinical practice, J. Adv. Pract. Oncol 10 (2) (2019), 10.6004/jadpro.2019.10.2.7.

[50]. Donovan KA, Grassi L, McGinty HL, Jacobsen PB, Validation of the distress thermometer worldwide: state of the science, Psycho-Oncology 23 (3) (2013) 241–250, 10.1002/pon.3430. [PubMed: 25160838]

[51]. Schellekens MP, Van den Hurk DG, Prins JB, Molema J, Van der Drift MA, Speckens AE, The suitability of the hospital anxiety and depression scale, distress thermometer and other instruments to screen for psychiatric disorders in both lung cancer patients and their partners, J. Affect. Disord 203 (2016) 176–183, 10.1016/j.jad.2016.05.044. [PubMed: 27295374]

[52]. Snaith RP, Zigmond AS, The hospital anxiety and depression scale, BMJ 292 (6516) (1986) 344, 10.1136/bmj.292.6516.344.

[53]. Kertz SJ, Lee J, Bjorgvinsson T, Psychometric properties of abbreviated and ultra-brief versions of the Penn State Worry Questionnaire, Psychol. Assess 26 (4) (2014)1146–1154. [PubMed: 24932640]

[54]. Meyer T, Miller M, Metzger R, Borkovec TD, Development and validation of the Penn State worry questionnaire, Behav. Res. Ther 28 (6) (1990) 487–495, 10.1016/0005-7967(90)90135-6. [PubMed: 2076086]

[55]. Trapnell PD, Campbell JD, Private self-consciousness and the five-factor model of personality: distinguishing rumination from reflection, J. Pers. Soc. Psychol 76 (2) (1999) 284–304, 10.1037/0022-3514.76.2.284. [PubMed: 10074710]

[56]. Derryberry D, Reed MA, Anxiety-related attentional biases and their regulation by attentional control, J. Abnorm. Psychol 111 (2) (2002) 225–236, 10.1037/0021-843x.111.2.225. [PubMed: 12003445]

[57]. Gross JJ, John OP, Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being, J. Pers. Soc. Psychol 85 (2) (2003) 348–362, 10.1037/0022-3514.85.2.348. [PubMed: 12916575]

[58]. Ouellet-Morin I, Danese A, Arseneault L, Validation of a high-sensitivity assay for C-reactive protein in saliva, Brain Behav. Immun 24 (2010) S8–S9, 10.1016/j.bbi.2010.07.027.

[59]. Chiang JJ, Eisenberger NI, Seeman TE, Taylor SE, Negative and competitive social interactions are related to heightened proinflammatory cytokine activity, Proc. Natl. Acad. Sci 109 (6) (2012) 1878–1882, 10.1073/pnas.1120972109. [PubMed: 22308464]

[60]. Weik U, Herforth A, Kolb-Bachofen V, Deinzer R, Acute stress induces proinflammatory signaling at chronic inflammation sites, Psychosom. Med 70 (8) (2008) 906–912, 10.1097/psy.0b013e3181835bf3. [PubMed: 18799429]

[61]. Johannsen A, Rydmark I, Söder B, Åsberg M, Gingival inflammation, increased periodontal pocket depth and elevated interleukin-6 in gingival crevicular fluid of depressed women on long-term sick leave, J. Periodontal Res 42 (6) (2007) 546–552, 10.1111/j.1600-0765.2007.00980.x. [PubMed: 17956468]

[62]. Cameron SO, Carman WF, The use of the OraSure® collection device for hepatitis virus testing in health care settings, J. Clin. Virol 34 (2005) S22–S28, 10.1016/s1386-6532(05)80006-x. [PubMed: 16461219]

[63]. Nicolson NA, Measurement of cortisol, in: Luecken LJ, Gallo LC (Eds.), Handbook of Physiological Research Methods in Health Psychology Thousand Oaks, Sage Publications, Inc, CA, US, 2008, pp. 37–74.

[65]. Given CW, Given B, Stommel M, Collins C, King S, Franklin S, The caregiver reaction assessment (CRA) for caregivers to persons with chronic physical and mental impairments, Res. Nurs. Health 15 (4) (1992) 271–283. [PubMed: 1386680]

[66]. Nijboer C, Tempelaar R, Triemstra M, van den Bos GA, Sanderman R, The role of social and psychologic resources in caregiving of cancer patients, Cancer. 91 (5) (2001) 1029–1039. [PubMed: 11251956]

[67]. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN, The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research, Arthritis Rheum. 49 (2) (2003) 156–163. [PubMed: 12687505]

[68]. Cella D, Riley W, Stone A, et al. , The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008, J. Clin. Epidemiol 63 (2010) 1179–1194. [PubMed: 20685078]

[69]. Hays RD, Bjorner JB, Revicki DA, et al. , Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items, Qual. Life Res 18 (2009) 873–880. [PubMed: 19543809]

[70]. Applebaum AJ, Panjwani AA, Buda K, O'Toole MS, Hoyt MA, Garcia A, Fresco DM, Mennin DS, Emotion regulation therapy for cancer caregivers – an open trial of a mechanism-targeted approach to addressing caregiver distress, Transl. Behav. Med 10 (2) (2020) 413–422. https://pubmed.ncbi.nlm.nih.gov/30395306/. [PubMed: 30395306]

[71]. Borkovec TDNS, Credibility of analogue therapy rationales, J. Behav. Ther. Exp. Psychiatry 3 (1972) 257–260.

[72]. Devilly GJ, Borkovec TD, Psychometric properties of the credibility/expectancy questionnaire, J. Behav. Ther. Exp. Psychiatry 31 (73–86) (2000).

[73]. Bjordal K, De Graeff A, Fayers PM, et al. , A 12 country field study of the EORTC QLC-C30 (version 3.0) and the head and neck cancer specific module (EORTC QLC-H and N35) in head and neck patients, Eur. J. Cancer 36 (2000) 1796–1807. [PubMed: 10974628]

[74]. Cohen S, Kamarck T, Mermelstein R, A global measure of perceived stress, J. Health Soc. Behav 385–396 (1983). [PubMed: 6668417]

[75]. Cohen S Perceived stress in a probability sample of the United States. In: Spacapan S & Oskamp S (Eds.), The Claremont Symposium on Applied Social Psychology. Thousand Oaks, CA, US: Sage Publications, Inc.

[76]. National Survey on Drug Use and Health (NSDUH): CAI Specifications for Programming (English Version), Rockville, MD: Center for Behavioral Health Statistics and Quality. Substance Abuse and Mental Health Services Administration, 2019.

[77]. Lichtenthal W, et al. Barriers to mental health/ service use among parents who lost a child to cancer. Paper Presented at: American Psychosocial Oncology Society 8th Annual Conference 2011; Anaheim, CA.

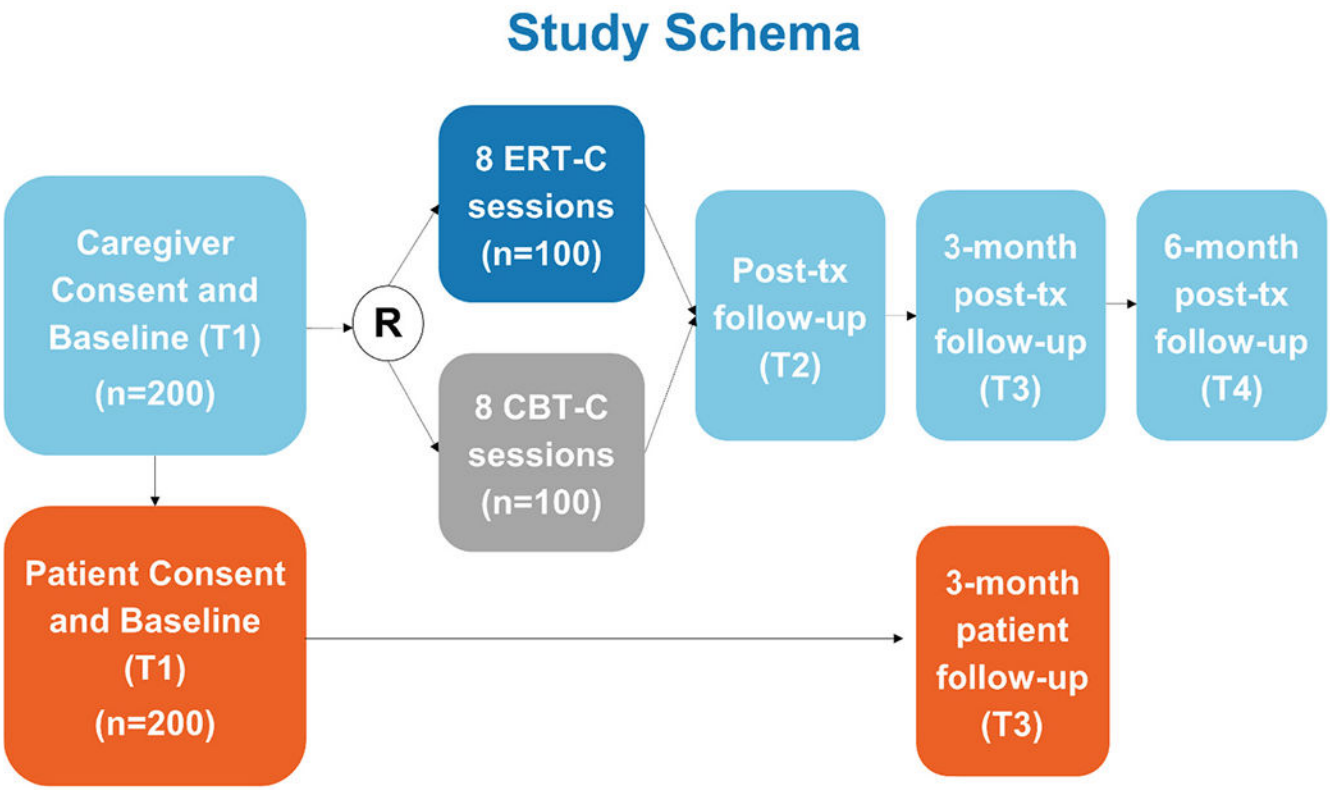

Fig. 1.
Study Schema.

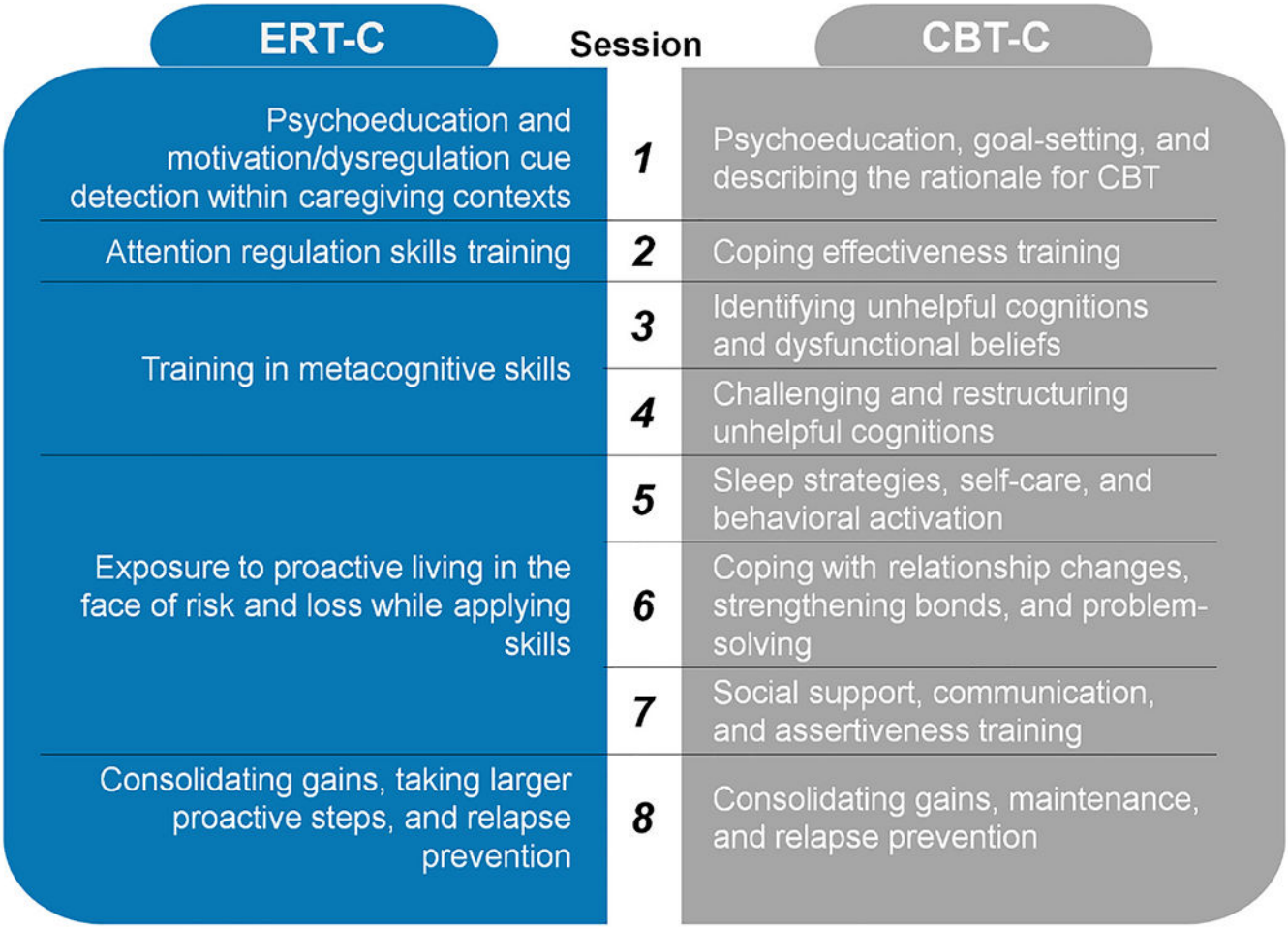

Fig. 2.
Session Summaries.

Table 1

Study Assessments and Timepoints.

Assessment	Domain	Timepoint Assessed					
		Caregiver				Patient	
		T1	T2	T3	T4	T1	T3
Demographic Information and Psychosocial Services Use, Preferences, and Perceived Barriers	Background and demographic information	X					
Distress Thermometer	Caregiver Distress	X	X	X	X		
Hospital Anxiety and Depression Scale	Anxiety and Depression	X	X	X	X		
Penn State Worry Questionnaire	Worry	X	X	X	X		
Rumination- Reflection							
Questionnaire, Rumination subscale	Rumination	X	X	X	X		
Attentional Control Scale	Attentional focus and shifting ability	X	X	X	X		
Experiences Questionnaire, Decentering subscale	Disidentification with negative thinking	X	X	X	X		
Emotion Regulation							
Questionnaire, Reappraisal subscale	Emotion regulation capacity	X	X	X	X		
Caregiver Quality of Life Index – Cancer	Quality of life	X	X	X	X		
Caregiver Reaction Assessment	Caregiver burden	X	X	X	X		
Self-Administered Comorbidity Questionnaire	Comorbid medical problems	X	X	X	X		
Patient-Reported Outcomes Measurement Information System Global Health Scale	Global mental and physical health.	X	X	X	X	X	X
Credibility and Expectancy Questionnaire	Expectation of treatment outcome		X				
EORTC QLQ-C30	Cancer patient quality of life					X	X
Perceived Stress Scale	Perceived stress					X	X
National Survey on Drug Use and Health, Healthcare Utilization	Healthcare service utilization					X	X
Working Alliance Inventory-Short form[a]	Therapeutic alliance						
Inflammatory Markers Assessment	IL-6, CRP, and sTNFαRII	X	X	X	X		
Diurnal Cortisol Assessment	Diurnal rhythm in salivary cortisol	X	X	X	X		

[a]The Working Alliance Inventory is administered after the fourth intervention session.