Protocol of a Randomized Trial of Acceptance and Commitment Therapy for Fatigue Interference in Metastatic Breast Cancer

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Abstract

Fatigue interference with activities, mood, and cognition is one of the most prevalent and distressing concerns of metastatic breast cancer patients. To date, there are no evidence-based interventions for reducing fatigue interference in metastatic breast cancer and other advanced

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cancer populations. In pilot studies, Acceptance and Commitment Therapy (ACT) has shown potential for reducing symptom-related suffering in cancer patients. The current Phase II trial seeks to more definitively examine the efficacy of telephone-based ACT for women with metastatic breast cancer who are experiencing fatigue interference. In this trial, 250 women are randomly assigned to either the ACT intervention or an education/support control condition. Women in both conditions attend six weekly 50-minute telephone sessions. The primary aim of this study is to test the effect of telephone-based ACT on fatigue interference. Secondary outcomes include sleep interference, engagement in daily activities, and quality of life. Outcomes are assessed at baseline, 2 weeks post-intervention, and 3 and 6 months post-intervention. This trial also examines whether increases in psychological flexibility, defined as full awareness of the present moment while persisting in behaviors aligned with personal values, account for the beneficial effect of ACT on fatigue interference. After demonstrating ACT's efficacy, the intervention can be widely disseminated to clinicians who care for metastatic breast cancer patients. Our findings will also inform future ACT trials with various cancer populations and functional outcomes.

Keywords: Acceptance and Commitment Therapy; fatigue; sleep; metastatic breast cancer; psychosocial intervention; symptom management

1. Introduction

Fatigue is a prevalent, persistent, debilitating symptom in metastatic breast cancer (MBC) patients [1-3]. Moderate-to-severe fatigue is reported by over 50% of MBC patients [1, 2]. Fatigue frequently co-occurs with a number of symptoms, such as sleep disturbance, cognitive

concerns, anxiety, and depressive symptoms [4, 5], resulting in impaired daily activities [1, 5, 6]. Evidence-based interventions for managing fatigue in MBC and other advanced cancer populations are lacking [7-9]. A Cochrane meta-analysis of pharmacologic interventions for fatigue in advanced cancer and other palliative care patients characterized the evidence as inconclusive and highlighted the small, heterogeneous samples in many studies [7]. Furthermore, of the five psychotherapy trials for MBC patients targeting fatigue [9], only a trial of year-long supportive-expressive group therapy effectively reduced fatigue [10]; importantly, this finding was not replicated by others [11]. Innovative approaches are therefore needed to reduce fatigue-related suffering and interference with functioning.

One behavioral intervention that shows potential for reducing symptom-related suffering in cancer patients is Acceptance and Commitment Therapy (ACT) [12, 13]. Rather than focusing on symptom reduction, the goal of ACT is to increase psychological flexibility so that difficult internal experiences (e.g., physical symptoms, feelings, thoughts) interfere less with meaningful activities [14, 15]. Psychological flexibility is comprised of mindfulness/acceptance processes (i.e., nonjudgmental attention to the present moment) and commitment/behavior change processes (i.e., identifying personal values such as family or work and taking action steps consistent with these values) [15]. ACT has been shown to reduce distress and pain interference in patients with chronic pain [16-19] and has been tested in pilot trials with cancer patients [13, 14, 20-22]. In our pilot RCT, MBC patients were randomized to six telephone sessions of either ACT or time-equivalent education/support [23]. ACT showed strong evidence of feasibility and promise with respect to fatigue and sleep interference with activities, mood, and cognition. Feasibility was demonstrated by the eligibility screening rate (64% of reached patients agreed to be screened) and the retention rate (83% [39/47] at 8 weeks post-intervention).

The primary aim of this NIH-funded Phase II RCT is to more definitively examine the efficacy of our telephone-based ACT intervention for women with MBC who have fatigue interference. We hypothesize that ACT will lead to an improved primary outcome of fatigue interference as compared to time-equivalent education/support. Our second aim is to test the effects of telephone-based ACT on the secondary outcomes of sleep interference, engagement in daily activities, and quality of life. We hypothesize that ACT will lead to superior secondary outcomes relative to education/support. Our third aim is to test the hypothesis that increased psychological flexibility will mediate ACT's effect on fatigue interference. Our fourth aim is to explore changes in the two core aspects of psychological flexibility (i.e., mindfulness/acceptance and commitment/behavior change processes) as mediators of ACT's effect on fatigue interference. The current paper describes the rationale, design, methods, and statistical plan for this RCT that aims to address a critical gap in comprehensive, evidence-based care for women with MBC.

2. Materials and Methods

2.1. Overview of study design

This Phase II RCT tests the effects of telephone-based ACT on fatigue interference and related outcomes in women with MBC. Our recruitment goal is 250 patients with moderate-to-severe fatigue interference. We recruited about six patients per month over 8 months in our pilot [23]. Assuming a similar recruitment rate, we will recruit 250 patients over 3.5 years. Patients are randomized to six weekly 50-minute telephone sessions of ACT or six weekly 50-minute telephone sessions of education/support. Outcomes are assessed at baseline, 2 weeks post-intervention (primary endpoint), and 3 and 6 months post-intervention. This trial was registered

in clinicaltrials.gov (NCT03998618) and approved by the Indiana University Institutional Review Board.

2.2. Participant eligibility criteria

Eligible patients meet the following inclusion criteria: a) ≥ 18 years old, b) at least 3 weeks post-diagnosis of Stage IV breast cancer as ascertained through medical records and consultation with the attending oncologist, and c) moderate to severe fatigue interference (i.e., mean score ≥2.5 on the Fatigue Interference subscale of the Fatigue Symptom Inventory [FSI]) [24, 25]. The clinical validity of this cut point is supported by our pilot research with MBC patients. Exclusion criteria include: a) significant cognitive impairment (dementia/delirium, psychosis) as ascertained by a medical record review and administration of a mental status questionnaire [26], b) patient-reported Eastern Cooperative Oncology Group (ECOG) score > 2 (spend most of the day in bed or chair) [27], c) enrolled in hospice, d) lack of English fluency, e) male, and f) no working phone service. Those with an ECOG score above 2 are excluded, as the ACT intervention is designed for those who can engage in at least moderate levels of activity.

2.3. Recruitment

Under an IRB-approved waiver of HIPAA authorization, study staff search electronic health records for patients with a diagnosis of MBC, along with the name of their primary oncologist. The primary oncologist reviews patient lists and indicates those whom we may contact about participation. Potentially eligible women are mailed a study introductory letter along with a consent form. The letter includes a phone number for those who have questions or wish to opt out of further contact from the study team.

A research assistant (RA) calls all patients who do not opt out approximately 1 to 2 weeks after the letter is mailed. The RA describes the study as outlined in the consent form, answers

questions, and administers a screening assessment (i.e., Fatigue Interference subscale of FSI [24, 25], ECOG [27], and mental status questionnaire [26]) with the patient's permission. Eligible and interested patients provide consent for study participation over the phone under a waiver of documentation of written informed consent.

2.4. Randomization and blinding

Following baseline assessments, patients are randomly assigned to ACT or education/support using stratified block randomization to balance the groups by age (<65 yrs. vs. ≥65 yrs.) and performance status (patient-reported ECOG scores 0 or 1 vs. 2 [27]). We are stratifying randomization by performance status because it is a key factor in MBC treatment decisions [28]. The statistician uses the R package "blockrand" [29, 30] to generate random assignments within blocks. Randomly varying block sizes of 2, 4, 6, and 8 are used to maintain allocation concealment and assure balanced allocation to study conditions. Following randomization, intervention assignments are identifiable to patients, interventionists, and staff mailing intervention materials. Other investigators, data monitoring committee members, outcome assessors, and data analysts are blinded throughout the trial.

2.5. Interventions

2.5.1. Acceptance and Commitment Therapy (ACT)

Study team members developed the ACT manual, which was informed by literature on fatigue and related symptoms in MBC patients [1, 2, 4], the ACT model [12, 15], previous ACT trials with patients with cancer and other chronic conditions [14, 17, 18, 20, 31, 32], and our clinical experience. Table 1 provides a summary of the intervention components. Grounded in the ACT model [15], the intervention is designed to reduce fatigue interference by increasing psychological flexibility, consisting of mindfulness/acceptance processes and

commitment/behavior change processes (see Figure 1: Conceptual Model). The mindfulness/acceptance component of psychological flexibility is targeted through mindfulness practices that facilitate non-reactive acceptance of fatigue-related thoughts, emotions, and bodily sensations. Willingness to experience the present moment courageously and flexibly is emphasized. Additionally, the commitment/behavior change component of psychological flexibility is targeted through identifying deeply held values (e.g., being a loving, engaged parent) and making behavior changes consistent with these values. Weekly value-based action goals are in the SMART format (Specific, Measurable, Achievable, Relevant, and Time-Bound). Thus, ACT emphasizes living consistently with one's values even when fatigued rather than focusing one's cognitive and physical energies on controlling fatigue. Although all patients learn the same set of skills, sessions are tailored to their unique cancer experience and other challenges. The therapist administers three items from the Fatigue Symptom Inventory (i.e., average fatigue and fatigue interference with general activity and enjoyment of life) [24, 25], two PROMIS anxiety items [33], and two PROMIS depression items [33] during each session. These reports allow the therapist to monitor fatigue and distress. The therapist also assesses and records the patient's home practice of mindfulness and other skills and ends with a discussion of practice for the week ahead. Handouts summarizing the topics of each session and recordings that our team developed to guide mindfulness practices are sent to patients.

2.5.2. Education/Support

The education/support condition was tested in our pilot feasibility trial [23] and is similar to controls in other cancer trials [34, 35]. Patients randomized to this condition discuss their concerns, including symptoms and other cancer-related stressors, with a therapist providing psychological support. The therapist directs patients to resources for practical and health

information and contact information for psychosocial services. Additionally, the same fatigue, depression, and anxiety assessments as those in the ACT condition are completed during each session [24, 25, 33]. Table 1 provides a summary of the education/support components. Sessions include an orientation to the patient's medical center and treatment team, education regarding common quality-of-life concerns and symptoms experienced by cancer patients, and an overview of medical center and community resources for addressing these concerns. Therapists also describe resources for addressing financial concerns and methods of evaluating health information available via the Internet and other modalities. Education/support patients receive handouts summarizing the topics of each session and are asked to review them as homework. ACT concepts are not discussed.

2.5.3. Intervention training and supervision

Therapists are doctoral level psychologists or advanced doctoral students in clinical psychology with extensive training and experience delivering ACT or supportive counseling. Different therapists deliver each intervention to prevent cross-contamination between study conditions. Therapists received initial education in MBC diagnosis and treatment, psychological distress, and either ACT or supportive counseling techniques with training protocols developed in previous studies. Initial training also included role-plays of sessions detailed in manuals. All sessions are digitally recorded, and licensed psychologists and advanced doctoral students in clinical psychology randomly select recordings to review for adherence to the manual using checklists developed in our pilot work. Individuals monitoring adherence have expertise in ACT or supportive counseling techniques and received training in fidelity monitoring. During regular supervision with therapists, treatment adherence scores (number of required topics and exercises

covered in each session/total number of fidelity criteria) are provided and treatment fidelity issues are discussed. Therapists implement the feedback in subsequent sessions.

2.6. Retention

A number of strategies are used to increase study retention. All study staff, including RAs and therapists, have been trained to clearly communicate expectations to patients and to offer the option of completing follow-ups if they do not adhere to the intervention. Use of the telephone for all assessments and the intervention reduces barriers to participation for rural residents and those with low incomes. Text, phone, or email reminders are sent to patients prior to appointments. Patients receive $40 in gift cards to a major retailor for participating in each of the four assessments, for a possible total of $160 in gift cards.

2.7. Study measures and data collection schedule

Study measures and the data collection schedule are found in Table 2. Measures equate to a 35-minute baseline assessment and three, 30-minute follow-up assessments conducted by research assistants blind to study condition. All measures have evidence of reliability and validity in cancer patients.

2.7.1. Primary outcome: fatigue interference

The primary outcome measure is the 7-item Fatigue Interference subscale of the FSI [24, 25]. Items are rated on 11-point scales (0 = *no interference*; 10 = *extreme interference*) that assess the extent to which fatigue in the past week interfered with general level of activity, ability to bathe and dress, normal work activity (including housework), ability to concentrate, relations with others, enjoyment of life, and mood.

2.7.2. Secondary outcomes

Sleep interference is assessed with the 8-item Patient-Reported Outcomes Measurement Information System (PROMIS) sleep-related impairment measure [36, 37]. This measure evaluates the perceived interference of sleep problems with activities, mood, and cognition. *Engagement in daily activities* is assessed with the 6-item PROMIS short-form measure of ability to participate in social roles and activities [38]. The items, which are reverse-coded, measure difficulty engaging in social and recreational activities as well as usual work (including housework). *Quality of life* is measured with the 27-item Functional Assessment of Cancer Therapy-General (FACT-G), consisting of four subscales: Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, and Functional Well-Being [39]. An overall score is computed to represent general quality of life.

2.7.3. Mediators

Psychological flexibility, as measured by the 7-item Acceptance and Action Questionnaire-II (AAQ-II) [40], is assessed as a hypothesized mediator of the intervention's effect on fatigue interference. The two core components of psychological flexibility are also assessed as exploratory mediators. First, *mindfulness/acceptance* is measured by the 10-item Cognitive and Affective Mindfulness Scale-Revised (CAMS-R) [41]. The scale provides a comprehensive assessment of mindfulness processes, including attention, present-focus, awareness, and acceptance/non-judgement. Second, *commitment/behavior change* is measured by the 5-item Value Progress subscale of the Valuing Questionnaire [42]. This subscale assesses progress in living consistently with personal values.

2.7.4. Descriptive variables

To characterize the sample, we assess standard demographics and medical factors. Self-reported medical comorbidities are assessed via a checklist of nine chronic health conditions

[43]. Functional status is measured with the 1-item Patient Generated Subjective Global Assessment (PG-SGA), a patient-reported version of the ECOG score [27]. Cancer information, such as time since diagnosis and treatments, is assessed via chart review. Additionally, seven self-report items assess physical and mental healthcare use, including outpatient and emergency room visits, use of alternative healthcare services, and (at baseline only) prior mindfulness training [43, 44]. Patients also report their prescribed and over-the-counter medications. Finally, measures of symptom severity are administered. Fatigue severity and frequency are measured with six items from the FSI [24, 25], and sleep disturbance, cognitive concerns, anxiety, and depressive symptoms are each assessed with a 6-item PROMIS measure [33, 36, 37, 45-47]. Pain is assessed with 3-item and 4-item PROMIS measures of severity and interference, respectively [45, 48]. The extent to which hot flashes interfere with aspects of quality of life is evaluated with the 10-item Hot Flash Related Daily Interference Scale [49].

3. Statistical Analyses

3.1. Preliminary analyses

Distributional issues. Univariate and descriptive analyses will be performed on all dependent variables, and if necessary, normalizing and/or variance stabilizing transformations will be applied to the data before inferential analyses are undertaken. *Missing data/attrition*. We anticipate some missing data due to participant death, medical factors, and other reasons. For individuals who complete the first assessment but withdraw from the study, we will examine demographic, medical, and symptom factors that might be predictive of dropout using logistic regression. In the analyses for Aims 1 and 2 described below, all randomized participants will be included in intent-to-treat analyses [50], as the aims are concerned with the impact of the intervention on outcomes regardless of study completion status. Second, for participants who

miss assessments, it is possible that attrition may be related to the study condition to which they have been assigned. We plan to use the random effects pattern-mixture model proposed by Hedeker and Gibbons [51] to address missing data. *Analyses of potential covariates*. Because patients will be randomly assigned to study conditions, significant differences in baseline values of all measured variables are not expected. Even so, we will assess for differences in baseline factors (e.g., demographic, medical and healthcare use variables, symptom levels) between study conditions [52]. Any differences will be taken into account when interpreting results, and factors that differ between the groups will be included as covariates in sensitivity analyses.

3.2. Analysis for aim 1

A linear mixed-model repeated measures approach will be used to test the hypothesis that ACT will improve fatigue interference as compared to the education/support condition. The model will include the main effect of time (as categorical) and study group (ACT vs. education/support) and the time-by-study group interaction. A treatment effect will be evidenced by a significant interaction between time and study group. If the treatment effect is significant, follow-up tests will be conducted to examine group differences at each follow-up, controlling for the outcome at baseline.

Our sample size is calculated based on the estimated difference between study conditions (ACT vs. education/support) on the primary outcome of fatigue interference at 2 weeks post-intervention. In our pilot study, we found a moderate effect (d = -.30) of study condition on fatigue interference at 1 month post-intervention [23]. It should be noted that only about half of the pilot sample had elevated fatigue interference at baseline (unlike the present study, the pilot study did not require all eligible patients to have clinically significant levels of fatigue interference); thus, the effect size is likely to be higher in the present study where the sample will

have uniformly elevated fatigue interference at study entry. Indeed, among patients with moderate to severe baseline fatigue interference in our pilot study, we found a strong effect (d = -.59) of study condition on fatigue interference at 1 month post-intervention. Thus, we conservatively estimate a medium effect size of d = -.40 at 2 weeks post-intervention. With a sample size of 198 patients at 2 weeks post-intervention (assuming 21% attrition based on our pilot [23]), we will have 80% power (p = .05, two-tailed) to detect a Cohen's d of -.40 in a linear mixed model [53]. At the final, 6-month follow-up with a sample size of 163 (assuming 35% attrition), we will have 80% power (p = .05, two-tailed) to detect a Cohen's d of -.44 [53]. The estimated attrition is based on our promising feasibility data for telephone-based ACT [23], use of telephone assessments to maximize compliance, and MBC survival rates [54].

We will use established minimal clinically important differences (MCIDs) on the FACT-G total score and subscale scores as anchors for determining a MCID in fatigue interference. MCIDs for MBC and other cancer patients are 2-point differences on the FACT-G subscale scores and a 5-point difference on the FACT-G total score, which fall in the range of .3 to .5 SDs [55, 56]. We will calculate mean changes in fatigue interference from baseline to 2 weeks post-intervention corresponding with established MCIDs on the FACT-G. Then effect sizes for these mean changes will be computed. Although MCIDs have yet to be determined for measures of fatigue interference, guidelines on MCIDs for pain interference and quality-of-life measures suggest that an effect size of .5 (.5 SD) is clinically meaningful [57-60]. The current trial is powered to detect this effect size.

3.3. Analysis for aim 2

Linear mixed models will be run to test the hypothesis that ACT will improve the secondary outcomes of sleep interference, engagement in daily activities, and quality of life as compared to

the education/support condition. Each model will include the main effect of time (as categorical) and study group and the time-by-study group interaction. A treatment effect will be evidenced by a significant interaction between time and study group. The Sidak adjustment for correlated multiple outcomes will be used to control the familywise Type I error rate. If treatment effects are significant, follow-up tests will be conducted to examine group differences at each follow-up, controlling for the outcome at baseline.

3.4. Analysis for aim 3

The PROCESS macro developed by Andrew Hayes [61] will be used to test the hypothesis that increased psychological flexibility will mediate the effect of ACT on fatigue interference. The macro employs ordinary least squares regression. Bootstrapped confidence intervals will be computed for the indirect effect of study group on fatigue interference at 2 weeks post-intervention (via change in psychological flexibility over the same time period). Each analysis will control for baseline levels of the mediator and outcome. We tested for mediation at 2 weeks because this is the primary endpoint.

3.5. Analysis for aim 4

The PROCESS macro [61] will be used to explore the extent to which changes in mindfulness/acceptance and commitment/behavior change processes mediate (uniquely and collectively) the effect of ACT on fatigue interference. Both potential mediators will be entered into the same model. Bootstrapped confidence intervals will be computed for the indirect effect of study group on fatigue interference at 2 weeks post-intervention (via change in mindfulness/acceptance and commitment/behavior change processes over the same time period). The analysis will control for baseline levels of the mediators and outcome.

3.6. Exploratory analyses

To inform future research, we will explore the extent to which sociodemographics (e.g., age, education) and clinical characteristics (e.g., cancer treatments, baseline severity of fatigue and other symptoms, healthcare use) moderate the effects of ACT on primary and secondary outcomes. For these analyses, we will use linear mixed modeling at a two-sided significance level of 0.05. Preliminary findings or hypotheses generated from these moderation analyses will be further tested in a future trial.

4. Discussion

The current trial addresses the top-rated concern of MBC patients—fatigue interference with activities, mood, and cognition [1, 3]. Fatigue has a substantial negative impact on their daily activities [1, 5]. Evidence-based interventions for fatigue interference are lacking. The ACT model [15] and our pilot data [23] provide strong justification for the current trial. In our pilot RCT, telephone-based ACT was highly feasible and acceptable to MBC patients and had a moderate effect on fatigue interference relative to an education/support condition; an even larger effect was observed in the subsample with elevated baseline fatigue interference [23]. To our knowledge, there is only one published large-scale trial of ACT in cancer, which focused on health behavior change in colorectal cancer survivors [62].

ACT is well-suited to address fatigue interference in cancer patients, as it emphasizes acceptance of the present moment (mindfulness), including internal experiences such as fatigue, and engagement in activities consistent with personal values [12]. The use of a fatigue interference inclusion criterion allows us to target those most in need of intervention—an approach rarely used in the broader literature on behavioral interventions for fatigue [63]. Another noteworthy feature of this trial is that it tests theory-driven mediators of ACT's effects. Only 3% of psychosocial intervention trials in cancer have analyzed potential mediators of

intervention effects [64]. According to the ACT model, increased psychological flexibility is the primary mechanism underlying the beneficial health effects of ACT [15]. The core components of psychological flexibility are mindfulness/acceptance processes and commitment/behavior change processes. In prior studies with adults, psychological flexibility mediated the effects of ACT on mental health outcomes [65, 66]. If increases in overall psychological flexibility mediate ACT's effect on fatigue interference, then this finding would support a key aspect of the ACT model [15].

Additionally, we will explore whether change in the aforementioned core components of psychological flexibility mediate ACT's effect on fatigue interference. If our analysis shows that one component is driving ACT's effect, then the intervention could be modified in future trials to focus on this mechanism. For example, if commitment/behavior change processes more strongly mediate ACT's effect than does mindfulness/acceptance, this would provide a rationale for emphasizing these processes in future trials.

Our ability to demonstrate ACT's efficacy will lead to dissemination of this intervention to clinicians serving MBC patients, thereby addressing a critical gap in the evidence-based care of this rapidly growing population. This trial will also lay the groundwork for further application and testing of ACT on different functional outcomes and with a wide range of cancer populations.

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Table 1
Summary of Core Components of Each Intervention Condition

Acceptance and Commitment Therapy	**Education/Support**
• Identify current attempts to control fatigue and their impact on quality of life • Practice mindfulness with the therapist during sessions and at home (e.g., awareness of the breath, body scan, noticing sounds). • Practice cognitive defusion—learning to notice thoughts, feelings, and symptoms rather than being overwhelmed by them (e.g., passengers on the bus metaphor) • Observe and detach from fatigue and related thoughts and emotions to cultivate a transcendent sense of self from which to observe and accept changing experience. Willingness to experience the present moment with courage and flexibility is emphasized. • Identify key values (e.g., being a	• Orient patient to the medical center and treatment team; overview of quality of life concerns and discussion of physical quality of life and symptoms • Discuss common social challenges (e.g., talking with children about cancer and employment issues); tips on managing household challenges when ill; referral to resources for addressing social challenges • Discuss common emotional responses to cancer, including anxiety and depressive symptoms, and cognitive changes following cancer treatment; referral to mental health services • Describe common financial concerns related to cancer and its treatment; referral to resources for addressing financial challenges • Methods of evaluating health information on the Internet and other modalities • Review of prior session topics and referral to

loving partner, giving to one's community) • Goal setting and practice of value-based actions	websites with cancer-related information

Table 2
Measures and Timing of Data Collection

Domain	Measure	Baseline	2-weeks post-intervention	3-months post-intervention	6-months post-intervention
Primary outcome:					
Fatigue interference	Fatigue interference subscale of FSI	✓	✓	✓	✓
Secondary outcomes:					
Sleep interference	PROMIS short-form sleep-related impairment measure	✓	✓	✓	✓
Engagement in daily activities	PROMIS short-form measure of ability to participate in social roles and activities	✓	✓	✓	✓
Quality of life	FACT-G	✓	✓	✓	✓
Hypothesized mediator:					
Psychological flexibility	Acceptance and Action Questionnaire-II	✓	✓	✓	✓
Exploratory mediators:					
Mindfulness/Acceptance	Cognitive and Affective Mindfulness Scale-Revised	✓	✓	✓	✓
Commitment/Behavior change	Values Progress subscale of Valuing Questionnaire	✓	✓	✓	✓
Demographic and medical factors:					
Sociodemographics	Sociodemographics	✓			
Medical comorbidity	Checklist of 9 conditions	✓			
Functional status	Patient-reported ECOG	✓	✓	✓	✓
Cancer information (e.g., date of diagnosis, cancer treatments)	Chart review	✓	✓	✓	✓
Physical and mental healthcare use	Healthcare use interview	✓	✓	✓	✓
Medications	Medication interview	✓	✓	✓	✓
Severity of symptoms:					
Fatigue severity, sleep disturbance, cognitive concerns, anxiety, depressive symptoms, pain severity and interference, and hot flash interference	Fatigue severity and frequency items from FSI; PROMIS short-form measures of sleep disturbance, cognitive concerns, anxiety, depression, and pain	✓	✓	✓	✓

	severity and interference; Hot Flash Related Daily Interference Scale

Note. FSI = Fatigue Symptom Inventory; PROMIS = Patient-Reported Outcomes Measurement Information System; FACT-G = Functional Assessment of Cancer Therapy-General; ECOG = Eastern Cooperative Oncology Group.

Figure Caption

Figure 1. *Conceptual Model*

Note. Although psychological flexibility is a secondary outcome rather than a mediator in this pilot trial, our analyses will set the stage for formal mediation analyses in a future large-scale trial.