

Study design and protocol for tailored Acceptance and Commitment Therapy (ACT) to optimize quality of life in women living with metastatic breast cancer

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ABSTRACT

Women living with metastatic (stage IV) breast cancer face unique challenges, including arduous treatments, side effects, chronic symptom burden, and emotional distress. Nevertheless, most research has paradoxically focused on optimizing quality of life in women with early-stage, non-metastatic breast cancer. Acceptance and Commitment Therapy (ACT) is an evidence-based, third-wave cognitive behavioral therapy that focuses on creating 'a life worth living' by promoting meaning and purpose and optimizing quality of life. ACT may be particularly well-suited for women with metastatic breast cancer as it addresses salient existential concerns, while allowing for the co-occurrence of feelings of grief and loss that are normal and expected when facing a life-limiting prognosis. This manuscript describes the rationale and study design of a pilot randomized controlled trial to develop and assess the feasibility and acceptability of a tailored ACT intervention for women living with metastatic breast cancer. Participants (N = 30) will be randomized 1:1 to either ACT, cognitive behavioral stress management (CBSM), or a usual care control. Both ACT and CBSM are 8-week, group-based interventions that will be delivered online. Primary outcomes are rates of acceptance, retention, and satisfaction. Preliminary effects on variables of interest, including meaning and purpose, psychological flexibility, and several domains of quality of life, will also be examined. Findings will inform the conduct of a full-scale randomized controlled trial of our tailored ACT intervention in women living with metastatic breast cancer.

1. Introduction

According to the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Program [1], approximately one in eight women in the United States (12.9%) will receive a diagnosis of breast cancer in her lifetime. Of these diagnoses, 6–10% will be classified as de novo metastatic breast cancer (stage IV), i.e., breast cancer that has spread beyond the breast to other organs in the body (most commonly the bones, lungs, liver, and brain) at initial diagnosis [2]. However, metastatic breast cancer is most commonly diagnosed as a re-

currence when 20–30% of breast cancers initially diagnosed as non-metastatic subsequently become metastatic [3,4]. Although there is no cure for metastatic breast cancer, developments in life-prolonging and palliative treatments have significantly increased survival such that women may now live with metastatic disease for several years [5,6].

Nevertheless, women with metastatic breast cancer face unique challenges as they cope with life-limiting prognoses [7,8], including coping with uncertainty, loss of functioning, disruption of social/occupational roles, fear of death and suffering, concern for loved ones, and communication with healthcare providers. Women also experience sig-

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nificant symptoms and side effects related to breast cancer-specific treatments, including hot flashes, joint pain, neuropathy, vaginal dryness, sexual dysfunction, and issues regarding body image and feminine identity [9–11]. Importantly, individuals with metastatic cancer also cite the importance of finding meaning in one's life and in the cancer experience [7,12]. The unique role that protective factors, such as meaning and purpose, positive mood, and life satisfaction, play in optimizing quality of life [13–16] has resulted in a shift away from focusing solely on reducing distress in individuals coping with stressful life experiences like cancer [17–19].

Unlike more traditional cognitive behavioral therapies (CBT), Acceptance and Commitment Therapy (ACT) does not aim to challenge or change distressing thoughts or emotions related to stressful life events like cancer, but rather focuses on creating 'a life worth living' by promoting meaning and purpose through engagement in activities aligned with patients' core values [20–23]. Given that patients with metastatic cancer cite shifting priorities and the importance of finding meaning in the cancer experience [7,24], this approach may be particularly well-suited for women living with metastatic breast cancer as it addresses salient existential concerns, such as the loss of meaning and purpose [25–27], while allowing for the co-occurrence of feelings of grief and loss that are normal and expected when facing a life-limiting prognosis [7]. ACT is an evidence-based intervention that improves mood and quality of life [20–22,28]. However, despite its well-established benefits in non-cancer populations and burgeoning interest in its potential utility in the cancer context [29–31], there is a notable paucity of research examining the effects of ACT in cancer patients and survivors.

Emerging evidence suggests that ACT may improve quality of life and reduce distress like fear of recurrence in early-stage breast cancer survivors following primary treatment completion [32–34]. However, research in women living with metastatic breast cancer has been very limited. In a pilot study by Mosher and colleagues [35], women with metastatic breast cancer who participated in a 6 week, telephone-based ACT intervention demonstrated a decrease in fatigue and sleep-related impairment compared to an educational control. To our knowledge, no previous study has conducted focus groups in order to systematically develop and tailor an ACT protocol to address concerns specific to women living with metastatic breast cancer. Furthermore, previous ACT trials in the cancer context have employed either educational controls [34–36] or usual care/no control [32,33] rather than test the effects of ACT against an existing, evidence-based intervention like cognitive behavioral stress management (CBSM). CBSM is a standardized CBT-based stress and relaxation management intervention with strong evidence for improving quality of life in women with breast cancer [37–43] and is an ideal, more stringent comparator for ACT. ACT has also never been adapted for online delivery in order to remove barriers to participation among individuals with cancer.

The aim of this study is to develop and assess the feasibility and acceptability of an ACT intervention tailored to meet the needs of women living with metastatic breast cancer. Due to the physical and functional limitations associated with living with metastatic disease, both ACT and CBSM will be group-based interventions delivered online to facilitate access and participation. The tailored ACT intervention will combine structured, evidence-based practices with therapeutic processes inherent to peer discussion and support in group settings. This manuscript describes the procedures and methodology of a randomized three-arm pilot trial that compares the tailored ACT intervention to both CBSM and usual care in women with metastatic breast cancer (N = 30). Primary outcomes are rates of acceptance, retention, and satisfaction. Preliminary effects on variables of interest, including meaning and purpose, psychological flexibility, and several domains of quality of life, will also be examined.

2. Material and methods

2.1. Overview of study design

This study is a randomized three-arm pilot trial to evaluate the feasibility and acceptability of a tailored ACT intervention relative to CBSM and a usual care control among women living with metastatic breast cancer (N = 30). Upon enrollment and completion of a baseline assessment, participants will be individually randomized 1:1 to either ACT, CBSM, or usual care. Patients randomized to either ACT or CBSM will participate in eight, 90-min online intervention sessions conducted by a trained facilitator via a highly secure, HIPAA-compliant videoconference site (WebEx). Participants in all three conditions will complete four psychosocial assessments online: baseline, 4 weeks (mid-intervention), 8 weeks (immediately post-intervention), and 12 weeks (one month follow-up). Please see Fig. 1 for study schema. Women will be compensated \$50 per completed assessment (\$200 for completion of all four assessments). All procedures and questionnaires have been approved by the Northwestern University Institutional Review Board (IRB).

2.2. Participant eligibility

Participants (N = 30) will be women diagnosed with stage IV (M1) breast cancer at the Northwestern University Robert H. Lurie Comprehensive Cancer Center. Inclusion criteria: 1) female, 2) age ≥ 18 years, 3) diagnosis of metastatic (stage IV) breast cancer via physician diagnosis and confirmed via electronic medical record review, 4) able to speak and read English, 5) able to provide informed consent. Exclusion criteria: 1) severe or impairing psychiatric disorder that would limit compliance with study requirements, 2) diagnosis of early-stage/non metastatic breast cancer (stages I-III). Patients may have had any form of cancer treatment (surgery, hormone therapy, radiation, chemotherapy, or some combination thereof), or no cancer treatment.

2.3. Recruitment and enrollment

Multiple methods of recruitment will be employed including (a) consent to contact lists from the Northwestern University Enterprise Data Warehouse service or other Northwestern University investigators; (b) metastatic breast cancer support groups hosted by Robert H. Lurie Comprehensive Cancer Center of Northwestern University; and (c) community-based organizations (e.g., Gilda's Club). Women identified by electronic medical records will receive a letter and study flyer introducing the study at least one week prior to a recruitment phone call from study staff. Members of support groups and community-based organizations will be sent an email introducing the study with an attached flyer and provided with contact information for the study coordinator. Potential participants will undergo eligibility screening over the phone with study staff. Those who are eligible and interested will provide informed consent online.

3. Interventions

Upon completion of the baseline assessment, participants will be randomized 1:1 to either ACT, CBSM, or a usual care control using a random number generator.

3.1. Intervention delivery

The ACT and CBSM are both group-based, manualized interventions that will be delivered once per week over the course of 8 weeks via WebEx, a HIPAA-compliant, web-based videoconferencing platform. Sessions will be facilitated by study team members who are licensed, master's- or doctoral-level therapists. Participants will receive printed

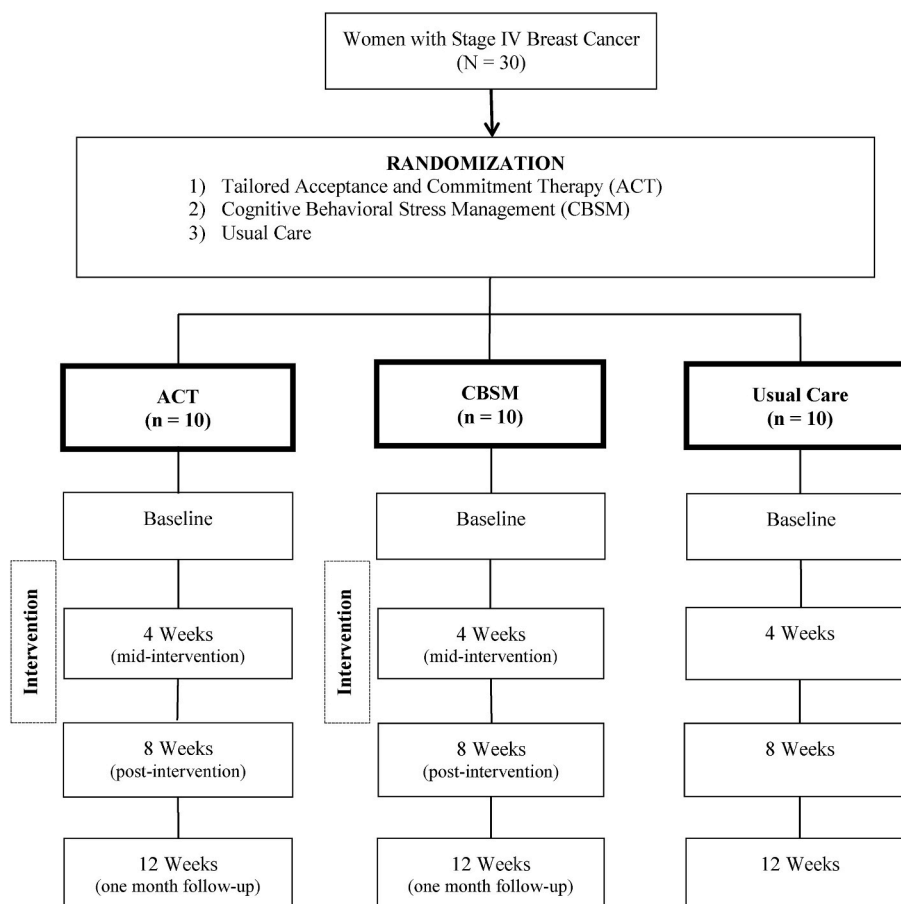


Fig. 1. Study schema.

workbooks prior to the first group session. Workbooks will include patient-facing intervention content for all eight sessions. Study staff also will conduct brief, remote tutorials with participants prior to the first group session to help participants log onto WebEx using a device of their choice (i.e., smartphone, tablet, laptop computer) to ensure they have access to intervention content, and to check audio and video connection. Participants who do not have a web-enabled device will be loaned a study tablet for the duration of the study. During each weekly group session, participants will have the opportunity to interact live with their group facilitator and fellow group members via WebEx video conferencing software. Participants will be able to keep their printed workbooks throughout the study duration and beyond. Women in ACT will not have access to the CBSM intervention content or workbook and vice versa.

Intervention sessions will be video recorded and study therapists will meet weekly with the principal investigator (PIM) throughout the 8 week duration of their groups in order to ensure fidelity to intervention protocols.

3.2. ACT intervention

Four focus groups with a total of 22 women living with metastatic breast cancer informed the development of the tailored ACT intervention. Women in the first two focus groups ($n = 12$) discussed psychosocial concerns and quality of life challenges related to living with metastatic breast cancer, as well as relevant topics of interest to be included in tailored intervention content, including stress, coping strategies, social support, body image, sexual functioning, and health behaviors. These data were used to create a draft of the ACT intervention protocol tailored for this population. Women in the second two focus

groups ($n = 10$) also provided discussed psychosocial concerns and quality of life challenges related to living with metastatic breast cancer and relevant topics of interest in addition to providing feedback regarding the proposed structure, content, and the online delivery of the ACT intervention protocol. Focus group discussions were 2 h in length and were audio recorded for transcription. Data were analyzed in Dedoose (version 8) [44] using a general inductive approach [45] to code upper- and lower-level categories and extract central themes in accordance with the NIH Best Practices for Mixed Methods Research in Health Sciences [46].

Based on thematic analysis of focus group data, JBT and PIM, both licensed clinical psychologists, developed an ACT intervention protocol that integrates core ACT principles and practices [23]: acceptance (non-judgmental awareness of internal and external experiences), cognitive defusion (noticing and gaining distance from thoughts), self as context (consistent, stable sense of self that is independent of experiences), values (identifying what is important and gives life meaning and purpose), committed action (taking action in order to build a life consistent with values), and mindfulness (awareness and contact with the present moment, often through focus on the breath). These processes are collectively known as psychological flexibility. Processes that deviate from psychological flexibility (experiential avoidance versus acceptance, cognitive fusion versus cognitive defusion, self as content versus self as context, lack of contact with values versus values identification, inaction versus committed action, lack of contact with the present moment versus mindfulness) are known as psychological inflexibility and are targeted as mechanisms of change in ACT [47].

Each group session includes a relevant mindfulness practice, explicit teaching and exercises based on a specific ACT process (50 min), and a themed group discussion relevant to the teaching of the day with non-

explicit interventions (45 min). Themed group discussions are designed to provide participants the opportunity to share their thoughts, feelings, and experiences regarding topics relevant to their experience living with metastatic breast cancer in order to foster a sense of connection and support between group members. Topics for themed group discussions were informed by thematic analysis of focus group data. Topics of themed group discussions by session include: 1) living with uncertainty, 2) the impact of cancer on identity, 3) coping with physical changes and body image, 4) navigating relationships with loved ones and the medical team, 5) navigating intimate relationships, 6) coping with loss, 7) self-care, and 8) bringing it all together and a life worth living. Please see Table 1 for ACT protocol content. In place of homework, participants will be encouraged to reflect during the week on what they learned in group and write down how this content applies to their day-to-day experiences in their participant workbook. Participants will also be given recordings of all in-session mindfulness exercises for additional independent practice between intervention sessions.

The developed ACT protocol is designed to deliver both explicit and non-explicit interventions. Explicit interventions include psychoeducation and didactic exercises that address core ACT processes, similar to the structure of most manualized cognitive behavioral therapies. Non-explicit interventions are used in-vivo when facilitators identify and address ACT processes as they occur during each session's themed group discussions. During themed group discussions, facilitators will intervene when they identify psychological inflexibility processes as they arise in the group discussion. Facilitators will observe inflexibility in both intrapersonal processes (within the member or facilitator, such as experiential avoidance) and interpersonal processes (between group members, or between the therapist and the group). When inflexibility processes arise, facilitators will utilize ACT-based interventions, such as non-judgmentally naming the process to the group (e.g., "I am noticing that ..."), posing a question to the group ("Is anyone in the group noticing ...?"), and modeling a psychologically flexible response (e.g., "I am aware that I am having the thought/feeling when ..." "How do you think (group member) might feel when you say ...?"). Facilitators will pay specific attention to ACT processes introduced during the psychoeducation and didactic exercises earlier in session so that they can be highlighted and reinforced during the themed group discussions. The inclusion of both explicit and non-explicit interventions is intended to bring together structured, evidence-based practices with the therapeutic processes inherent to peer discussion and support in group settings. Facilitators are expected to deliver both explicit and non-explicit interventions and content throughout the group experience. This structure is unique to many manualized therapies.

Table 1
Tailored acceptance & commitment therapy (ACT) protocol.

Week	Intervention Topic	Mindfulness Practices
1	Introducing Psychological Flexibility & Living with Uncertainty	Introduction to Mindfulness: Simple Breath Meditation
2	Values & the Impact of Cancer on Identity	Mindfulness: One Value Meditation
3	Acceptance & Coping with Physical Changes and Body Image	Mindfulness: Mountain Meditation
4	Distancing & Navigating Relationships with Loved Ones and Medical Team	Mindfulness: Leaves on a Stream Meditation
5	Mindfulness & Navigating Intimate Relationships	Mindfulness: Dropping an Anchor Meditation
6	The Observer Self & Coping with Loss	Mindfulness: Self-Compassion meditation
7	Committed Action & Self-Care	Mindfulness: Mindful Minute Meditation
8	Bringing it All Together & A Life Worth Living	Mindfulness: Relaxing Image Meditation

3.3. CBSM intervention

The CBSM intervention is based on a standardized, previously published protocol developed by Dr. Michael Antoni [48]. This protocol integrates core cognitive behavioral therapy principles and practices, such as cognitive restructuring (identifying and disputing irrational or maladaptive thoughts), behavioral activation (engagement in pleasant experiences, social activity, or experiences of mastery), and relaxation strategies like diaphragmatic breathing, progressive muscle relaxation, and meditation/imagery. Each group session includes a relaxation exercise and explicit teaching and exercises. Topics by session include: 1) introducing stress awareness and physical responses, 2) stress awareness and the appraisal process, 3) automatic thoughts and cognitive distortions, 4) cognitive restructuring and rational thought replacement, 5) coping, 6) social support, 7) anger management and assertiveness training, and 8) wrap-up and review. Please see Table 2 for CBSM protocol content. Participants are assigned weekly homework assignments to complete in their participant workbook. They will also be given recordings of all in-session relaxation exercises for additional independent practice between intervention sessions. In order to ensure that CBSM and ACT are dose-matched, the original 10-week CBSM protocol [48] was adapted to be delivered in eight weeks by merging similar intervention content across sessions. A detailed description of these changes is available upon request.

4. Data collection

4.1. Assessment timeline

Participants in all three conditions will complete four assessments online at baseline, 4 weeks (mid-intervention), 8 weeks (immediately post-intervention), and 12 weeks (one month follow-up). Survey links will be sent to participants via email using Qualtrics.

4.2. Measures

4.2.1. Feasibility and acceptability

Rates of enrollment, attendance, and retention will be calculated. Participants randomized to ACT and CBSM will also rate satisfaction with intervention content on Likert-type scales at 4 weeks (mid-intervention): "How relevant was the content in Sessions 1 to 4 to your experience living with metastatic breast cancer?" (1 = Not at all relevant, 5 = Extremely relevant); "How helpful were the coping strategies covered in Sessions 1 to 4?" (1 = Not at all helpful, 5 = Extremely helpful); "How satisfied were you overall with Sessions 1 to 4?" (1 = Not at all satisfied, 5 = Extremely satisfied). These questions will be repeated at 8 weeks (immediately post-intervention) in reference to Sessions 5 to 8. Two additional questions will be added at 8 weeks:

Table 2
Cognitive behavioral stress management (CBSM) protocol.

Week	Intervention Topic	Relaxation Practices
1	Introducing Stress Awareness & Physical Responses	7 Muscle Group Progressive Muscle Relaxation (PMR)
2	Stress Awareness & the Appraisal Process	Diaphragmatic Breathing & 4 Muscle Group PMR
3	Automatic Thoughts & Cognitive Distortions	Deep Breathing with Counting and PMR & Special Place Imagery
4	Cognitive Restructuring & Rational Thought Replacement	Autogenic Practice for Stress Reduction
5	Coping	Relaxation Exercise for Healing and Wellbeing & Light Meditation
6	Social Support	Deep Breathing & Color Meditation
7	Anger Management & Assertiveness Training	Softening Meditation
8	Wrap-up & Review	Enchanted Cove Imagery

“How likely are to continue to use the skills and strategies you learned in Sessions 1 to 8?” (1 = Not at all likely, 5 = Extremely likely); “How helpful were the weekly reflections [for ACT]/at-home exercises [for CBSM] offered at the end of each session?” (1 = Not at all helpful, 5 = Extremely helpful). Open-ended questions will be used to assess what participants believe was the most and least valuable part of Sessions 1 to 4 at 4 weeks (mid-intervention) and Sessions 5 to 8 at 8 weeks (immediately post-intervention). Open-ended questions will also be used to solicit feedback regarding content in each session (e.g., “Session 1 focused on introducing psychological flexibility and living with uncertainty, do you have any feedback regarding this session or its content?”).

4.2.2. Psychosocial assessments

Psychosocial assessments will be completed at baseline, 4 weeks (mid-intervention), 8 weeks (immediately post-intervention), and 12 weeks (one month follow-up).

Meaning and Purpose will be assessed using the 4-item NIH PROMIS® Meaning and Purpose Short Form 4a [49]. *Quality of life* will be assessed using two measures: the 31-item NIH PROMIS® 29 + 2 Profile [50] and the 37-item Functional Assessment of Cancer Therapy-Breast (FACT-B) [51]. The NIH PROMIS® 29 + 2 Profile [50] assesses anxiety, depression, pain interference and intensity, fatigue, and physical functioning, sleep disturbance, ability to participate in social roles and activities, and cognitive function (concentration and memory). FACT-B assesses physical, social, emotional, and functional wellbeing, and breast cancer-related symptom bother (e.g., hair loss, hot flashes, arm mobility/function). *Positive affect* will be assessed using the 15-item PROMIS® Positive Affect – Short Form 15a [52]. *Social support* will be assessed using three 4-item measures: the NIH PROMIS® Emotional Support Short Form 4a, Informational Support Short Form 4a, and Social Isolation- Short Form 4a [47].

Psychological flexibility will be assessed using the 7-item Acceptance and Action Questionnaire (AAQ-II) [53] and 4-item Open and Engaged State Questionnaire [54] to capture to skills targeted by ACT (i.e., engagement with deeply held values, vitality and fulfillment, conscious openness to emotions and experiences, including distress tolerance). These measures are scored such that higher scores indicate greater levels of psychological inflexibility or experiential avoidance. *Self-efficacy* will be assessed using the 13-item Measure of Current Status (MOCS) Self-Efficacy Scale Part A [38] to capture perceived confidence in using skills targeted by CBSM (i.e., ability to relax at will, recognize stress-inducing situations, restructure maladaptive thoughts, assert needs, choose appropriate coping responses).

4.2.3. Sociodemographic and medical characteristics

A sociodemographics questionnaire will be administered at baseline to assess age, education, annual household income, race, ethnicity, sexual orientation, relationship status, parental status, health insurance coverage, and comorbid conditions. Electronic health records will be reviewed to confirm cancer diagnosis and stage. Women will report metastatic breast cancer diagnosis date and type (recurrence versus de novo) and previous cancer treatments (i.e., surgery, radiation, chemotherapy, hormone therapy, immunotherapy, other) at baseline. Women will also report current cancer treatments at each assessment.

4.2.4. Supportive care services

Current and previous use of supportive care services, including support groups and individual counseling, will be assessed at baseline. For women who are currently attending support groups and/or receiving individual counseling, frequency of services will be assessed (once per week or more often, every other week, once per month, less than once per month). Current and previous receipt of Cognitive Behavioral Therapy (CBT) or Acceptance and Commitment Therapy (ACT) will also be assessed at baseline. For women who are currently receiving CBT and/

or ACT, frequency of therapy will be assessed (once per week or more often, every other week, once per month, less than once per month).

4.3. Analytic plan

Rates of enrollment, attendance, and retention will be reported as percentages. Descriptive statistics will be used to summarize ratings of satisfaction using Likert-type scales. Responses to open-ended questions will be qualitatively coded for thematic analysis. Estimation of within-subjects intraclass correlations, effect sizes for change over time and between group differences, and within- and between-subject variability [55] in R 3.5.1 will contribute to power estimation for mixed model analyses to evaluate a future, full-scale randomized controlled trial. Previous work [56] demonstrates that minimally important differences for NIH PROMIS® measures in metastatic cancer patients are approximately 5 T-score points, which corresponds to a within-subjects Cohen's *d* of 0.5 [57]. Due to the small sample size of this study, statistical significance will be interpreted with caution and preliminary analyses of intended effects will primarily be used to estimate intervention effect sizes to calculate the sample size needed to adequately power a future, full-scale randomized controlled trial.

5. Discussion

The goal of this pilot randomized controlled trial is to develop and assess the feasibility and acceptability of an ACT intervention tailored to meet the needs of women living with metastatic breast cancer relative to CBSM and usual care. We will assess rates of enrollment, attendance, retention, and satisfaction as primary outcomes. We will also examine preliminary effects on variables of interest, including meaning and purpose, psychological flexibility, and several domains of quality of life. We hypothesize that the tailored ACT intervention will demonstrate adequate feasibility, including rates of enrollment, attendance, and retention at or above 80%. We hypothesize that women in the ACT and CBSM interventions will demonstrate greater improvements in quality of life, social support, and positive affect relative to usual care. Furthermore, we hypothesize that women in the ACT intervention will demonstrate greater increases in psychological flexibility and meaning and purpose relative to women in CBSM as these are ACT-specific intervention targets, whereas women in CBSM will demonstrate greater increases in self-efficacy using skills targeted by CBSM relative to women in ACT. Given the unique challenges of living with metastatic breast cancer [7,8,12], more research is needed to understand how to optimize quality of life and wellbeing in this patient population.

Strengths of this study include the conduct of focus groups to systematically develop and tailor an ACT intervention protocol to address concerns specific to women living with metastatic breast cancer. The creation of a group-based intervention that is designed to be delivered online using videoconferencing technology additionally helps remove barriers to participation, particularly during the COVID-19 pandemic. All study activities (i.e., informed consent, intervention, and assessments) will be conducted remotely online. Recruitment will also be conducted remotely via mailings and phone contact. Importantly, our three-arm randomized pilot trial includes an evidence-based intervention, CBSM [48], as a more stringent, dose-matched comparator to ACT and moves beyond solely including either educational controls [34–36] or usual care/no control [32,33]. The primary limitation of the current study is the small sample size, which may lead to insufficient power to observe between group differences. However, our sample size is consistent with feasibility and acceptability pilot trial design. Future studies should also develop behavioral and psychosocial interventions for men with metastatic breast cancer, another important and underserved patient population.

The current proposal addresses a crucial gap in the literature and has the potential to optimize quality of life among women coping with

the significant challenges associated with metastatic breast cancer. The long-term goal of this project is to use the findings from this pilot trial to conduct a high quality, full-scale randomized controlled trial and establish the efficacy of our tailored ACT intervention on quality of life and wellbeing. To our knowledge, this is the first study to develop and examine the feasibility and acceptability of an online, group-based ACT intervention tailored for women living with metastatic breast cancer.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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