Promoting Resilience in Women With Breast Cancer

University of Alabama at Birmingham

IRB #300011028

NCT #06133348

PI: Gabrielle Rocque, MD, MSPH

Study/Protocol Title: Promoting Resilience in Women with Breast Cancer

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Principal Investigator:

Gabrielle Rocque, MD, MSPH

UAB Medicine, Division of Hematology & Oncology

849 Boshell Building

1080 7th Ave South

Birmingham, AL 35294-3300

Phone: (205) 996-9281

Fax: (205) 934-7760

UAB Investigators:

Courtney Williams, DrPH (Statistical Lead)

Andres Azuero, PhD (Statistician)

Lily Gutnik, MD

Ritu Aneja, PhD

UAB Staff:

Stacey Ingram, MEd

Noon Eltoum, MBBS, MPH

Keynosis Hildreth, MPH

Etzael Ortiz, BS

D'Ambra Dent, MBA

Nicole E. Caston, MPH

1. Background and Significance

Patients with breast cancer often deal with persistent psychological distress. Fear of recurrence is associated with difficulties in performing daily and social activities, higher depression and anxiety, and lower quality of life.[1,2] These fears are not always unfounded. For example, among women with a substantial amount of residual disease after neoadjuvant chemotherapy, 40% will have recurrence of breast cancer by five years.[3] Fear of recurrence is more common in women with cancer who are younger, have children, and/or have fewer social supports.[4] Additionally, fear of recurrence is intensified among Black mothers with breast cancer compared to White mothers with breast cancer.[5] Furthermore, Black women are known to have a higher allostatic load (i.e., biological marker of stress),[6] which is associated, not only with higher likelihoods of breast cancer recurrence, but with overall worse quality of life during and after cancer-therapy.[7,8] Recent findings suggest that positive psychosocial experiences, including psychotherapeutic interventions and therapeutic mind-body protocols can modulate the inflammatory response by reducing the expression of genes/proteins associated with inflammation and stress-related pathways.[9] Interventions are urgently needed to support women at risk for recurent fear and distress, particularly marginalized populations who are vulnerable to experiencing disparate outcomes (e.g., progression, disability, death).

The PRISM (Promoting Resilience in Stress Management) intervention is an evidence-based program that builds resilience. This program was developed in adolescent and young adult oncology, and utilizes centrally-administered skills-based coaching to bolster positive psychological tools known as resilience resources. These resources include stress management, goal-setting, and positive reframing. Previous studies using this intervention have found PRISM to be successfully administered remotely and it has improved resilience, psychological distress, hope, and quality of life.[10] Among adult caregivers, PRISM has shown to improve resilience, self-efficacy, and engagement with medical care.[11] While PRISM successfully targets distress and associated downstream consequences known to be experienced by breast cancer survivors, it has not been utilized in adults with cancer or in marginalized communities. Adapting this intervention to this context will require the testing of the intervention and, importantly, tailoring to meet the needs of women with breast cancer, particularly those of marginalized populations who may uniquely benefit from this intervention.

2. Objective

This single-arm pilot study will (1) test feasibility, acceptability, and appropriateness of the PRISM intervention in individuals with breast cancer, (2) elicit patient perspectives on elements for future adaptation or expansion to meet the unique needs of women with breast cancer, (3) assess trajectory of patient-reported outcomes and biological measures of stress for patients with breast cancer receiving the PRISM intervention.

3. Hypothesis:

We hypothesize that PRISM will be feasible, acceptable, and appropriate for individuals with breast cancer.

4. Approach

3.1 *Study eligibility criteria, screening procedures, recruitment*: There will be two cohorts in this study. Cohort 1 will include women undergoing chemotherapy for early-stage breast cancer. Cohort 2 will include women undergoing treatment for metastatic breast cancer. Patients who do not speak English will be excluded. The study team will identify 30 women with early-stage disease (Cohort 1) and 10 women (Cohort 2) with metastatic disease to

participate through the review of daily clinic lists, coupled with discussions with clinical teams. We anticiapte minimal drop-out since patients will still be in an active phase of cancer treatment in the initial year after diagnosis. However, if patients drop out of the study, they will be replaced to achieve a total number of patients for each cohort. Across the entire study, we will sample such that we include at least 20 women who are Black or African American, ten women living in areas of higher disadvantage (defined using Area Deprivation Index), and five women with dependent children. Given the intersectionality of these characteristics, patients may represent more than one target population. Women will be approached in clinic by a study coordinator who will explain the study and obtain informed consent.

3.2 *Study Procedures-Patient and Clinic Characteristics:* A REDCAP database will be used to track patients approached, enrolled, and completing each portion of the study (blood/nail collection, patient reported outcomes (PROs), and intervention components). For patients enrolling in the study, a unique study ID will be created for each patients. The following patient and clinical characteristics of participants who enroll will be abstracted from the medical record: age at diagnosis, sex, race and ethnicity, insurance status, address, breast cancer stage, treatments received, BMI, blood pressure, prior diabetes/hypertension/cholesterol treatment. At the time of enrollment, a waist circumference will be captured using a tape measure (documented in cm).

Table 1. Promoting Resilience in Stress Management (PRISM) intervention content

Session Focus*	**Details**	**Format**	**Stress and Coping Theory Constructs**
1. Getting to Know You	Provide information about the logistics of the PRISM program, explain it in detail, and answer any questions the participant may have.	1:1 (video)	
2. Stress Management	Relaxation strategies (i.e., deep breathing), Mindfulness techniques	1:1 (video)	Situational factors
3. Catching Your Thought	Recognizing and reframing negative thoughts	1:1 (video)	Coping processes
4. Goal Setting	Setting SMART goals, planning for roadblocks	1:1 (video)	Situational factors
5. Finding the Positives	Identifying gratitude or meaning from illness experience	1:1 (video)	Coping processes
6. Coming Together	Discussion about what was learned, what worked, how loved ones can help (optional)	Family meeting (video)	Situational factors and Coping processes
Advance Care Planning	Discussion of advance care planning (optional)		
Skill Practice	Between-session exercises to practice, further develop and track skills	Digital app	

**Sessions 1-6 are delivered every 1-2 weeks.*

3.3 *Intervention:* PRISM is a manualized, brief, skills-based intervention targeting four resilience resources (stress-management, goal-setting, cognitive-reframing, meaning-making) consistently associated with improved psychosocial outcomes (**Table 1**).[10-12] Its content has been validated with proof-of-concept and pilot studies in diverse populations, including Adolescents and Young Adults (AYAs) with cancer, diabetes, or cystic fibrosis; parents of children with cancer or diabetes; interdisciplinary health-care professionals during the COVID-19 pandemic; adults with congenital heart disease; and caregivers of adult patients from marginalized background who experience racism.[79] The program has proven efficacy in randomized trials among these populations.[11,12] The content is understandable and applicable across multiple stressful situations, thus creating the potential for broad, ground-breaking impact. Content will all be provided by video.

Specifically, PRISM is delivered by trained intervention staff (called "coaches" within the PRISM program). Each coach receives >8 hours of standardized training, including role-playing and trouble-shooting, to demonstrate competency and mastery of the program script. Each PRISM session is audio-recorded to monitor for script-fidelity; the senior coach training reviews and scores each recording for fidelity using a standardized tool. In cases where coaches do not receive a score of 80% or higher, they receive additional training and supervision. In the history of the PRISM program's experience and >500 program deliveries, to date, no such remediation has yet been necessary.

Intervention sessions are described in detail in the attached Appendix A (PRISM manual). They are scheduled approximately weekly to every-other-week, depending on participant preference to optimize feasibility and completion. Briefly, for each session, coaches (i) ensure a private video conference to enable participation and conversation; (ii) review session content and format; (iii) teach and practice a particular resilience skill; and (iv) plan opportunities to practice the skill. Session 1, Stress-Management, involves mini-skills such as deep breathing, guided imagery, and mindfulness. Session 2, Goal-Setting, involves deconstructing and reconstructing goals to make them "SMART" (Specific, Measurable, Actionable, Realistic, and Time-Dependent). The session also includes exercises to plan for challenges and alternative strategies.Session 3, Cognitive Restructuring, involves recognizing negative self-talk and reframing impressions of negative experiences to make them feel more manageable. Session 4, Meaning-Making, involves exercises to find gratitude and purpose in the context of adversities like cancer. Session 5 (optional), Coming Together, is optional and involves the participant and their loved ones discussing the program and lessons-learned. Session 6 (optional) involved advance care planning to discuss future goals related to medical care.

Throughout the program, participants will have access to the award-winning PRISM smartphone app. This program provides practice opportunities for all of the skills, plus an embedded journal to catalogue goals, lessons-learned, and gratitudes; a library of related, evidence-based resources; tracking tools to monitor one's own stress and resilience.

The total PRISM intervention lasts 6-8 weeks, and the app is available thereafter, indefinitely.

3.4 *Study Procedures-Surveys:* Following enrollment, the participants will be asked to complete baseline surveys at the time of consent. The research coordinator will register the patient, providing the study ID, patient phone number, and email address for survey completion to the PRO Core team at the University of North Carolina. Surveys will be

completed electronically, when possible, but paper and telephone-based options will be available for patients not able to complete electronically. Baseline surveys should be completed within 90 days of completion of definitive therapy (chemotherapy, radiation, or surgery) for Cohort 1 (early stage) and at any time post metastatic diagnosis for Cohort 2 (metastatic). We will allow people to enroll during ongoing maintenance therapy with non-cytotoxic therapies including endocrine therapy, targeted therapy (e.g. Her2-targeted therapy) or immunotherapy. Patients will be asked to complete a follow-up survey after completion of the PRISM intervention, with a goal completion of within 60 days. We will make up to 5 attempts to reach patients if they do not complete their survey. The survey includes 114 questions at baseline and 106 questions at follow-up on feasibility, acceptability, appropriateness, recent stressors, fear of recurrence, anxiety, depression, social determinants of health, spirituality, resilience, posttraumatic growth, patient activation, and quality of life (**Table 2**). The survey is expected to take approximately 30-40 minutes to complete.

Survey responses will be captured using a database hosted by the University of North Carolina PRO Core. The staff at PRO Core will contact participants once prior to each survey due-date, and up to 4 times thereafter for missed surveys. PRO Core will oversee data monitoring and quality. PRO Core adheres to best practices for data security and privacy. PRO Core is accessed through a web interface using a secure, authenticated login. Data are stored in a secure enterprise-level Oracle database; the databases and web servers are hosted by the UNC Center for Bioinformatics. Data transmitted between the server and end-users are encrypted using SSL, and all databases are encrypted. PRO Core will story patient data in a secure database identified by a coded study ID. Upon study conclusion, the de-identified dataset will be transferred to UAB via secure transfer and stored in a password protected file for analysis.

3.5 Study Procedures- Biological Specimens (Cohort 1 Early Stage Breast Cancer Patients Only):

Blood samples:

Blood samples will be collected at baseline and approximately 6 months after surgery (post PRISM intervention, aligned with standard of care appointment where possible).

A trained phlebotomist will draw 25 mL of blood per draw (5 teaspoons) via standard venipuncture performed at pre and post assessments. A maximum of five 5 mL vials will be drawn from each participant per phlebotomy session. Samples will be labeled with a study ID and date of collection. Serum preparation analyses will use collection tubes with clot activators (ie.- red top tubes). Blood will be centrifuged at 4°C for approximately 10 minutes and sera will be aliquoted. Samples will be designated with study participant label only for specified analyses and stored in -80C until assays are performed.

When ready for analysis, serum samples will be delivered by the research coordinator to the Bio-Analytical Redox Biology (BARB) Core at UAB for mDAMPs analysis and to the NORC metabolic core at UAB for the blood based biomarkers in allostatic load analysis respectively. In addition, blood samples will be mailed to Eve technologies for analysis of inflammatory cytokines. .

Patients will also be asked if they are willing to have blood stored for future biomarker and omics evaluation. Additional sample preparation may be done on those blood samples, in

order to cryopreserve blood in appropriate forms for epigenetics, proteomics & transcriptomics evaluation. If patient declines, remaining biospecimens will be discarded.

Serum analyses:

1. Serum analyses for mtDNA DAMPs an nail cortisol will be performed at the Bio-Analytical Redox Biology (BARB) Core, UAB.
2. Serum analysis for allostatic load will be conducted at NORC metabolic core, UAB. These samples will be tested for serum cortisol, CRP, homocysteine, creatinine, albumin, lipid panel, and Hgb A1C.
3. Serum analysis of inflammatory markers IL-6 and TNF-alpha will be performed by the NORC metabolic core.

Nail sample collection and analysis: Cortisol measurements will also be derived from nail samples. Nail samples will be provided by participants using fingernail trimming clippers. They will be sent to the Bio-Analytical Redox Biology (BARB) Core at UAB for further analysis. Fingernails and toenails will be cut and stored independently until processed using the procedure previously described. Briefly, nail samples will be washed twice with 2 mL isopropanol and dried overnight. The dried nail samples will be added to a pre weighed tube containing three 5 mm steel grinding balls (Retsch) and ground using a TissueLyser II (Qiagen Venlo, Netherlands) at 30 Hz for 9 min. 1 mL of methanol will be added per 50 mg of powdered nail (w/v) and placed on a rotator for 18 h at room temperature to extract the cortisol. Samples were then centrifuged at 10,000 x g for 5 min. 800 µL of supernatant was transferred to a clean tube and evaporated under nitrogen gas in a certified fume hood. The evaporated sample will be resuspended in 400 µL of phosphate buffered saline per 50 mg of ground sample (w/v). Cortisol will be assayed using 25 µL of sample according to manufacturer's protocol (Salimetrics, Salivary Cortisol Enzyme Immunoassay Kit, 1-3002, State College, PA).

3.5 *Study Procedures- Intervention (Both Cohorts):* Following baseline survey and biospecimen collection, participants will schedule their PRISM sessions with study staff, who will also connect them with their coach. Staff and coaches will verify best contact methods and confirm timelines with participants. Coaches will provide a calendar of sessions as appointments. Staff and/or coaches will provide session reminders via phone, email, and/or text, based on participant preference, one day and 15-minutes prior to each session.

3.6 *Study Procedures- Post-intervention Interview* (*Both Cohorts*) Upon completion of the whole intervention, participants will participate in a 30 minute to 1-hour semi-structured interview (Appendix B) to elicit perspectives on psychological state, intervention feasibility and acceptability, and areas for expansion of the intervention to better meet the needs of women with breast cancer, all the while with a focus on equity. A semi-structured interview will be conducted by a trained qualitative interviewer either in person or virtually using Zoom or by phone based on patient choice. Interviews will be audio recorded, transcribed verbatim, and stored in a secure, password-protected folder. Participants who do not complete the intervention or complete surveys will also be asked to participate in interviews to explore barriers to completion and opportunities for improvement.

Table 2. Primary and secondary outcomes.					
Domain	**Instrument or Source**	**Baseline**	**Follow-up**	**Number of items**	**Expected length of time to complete**
Demographics	Study-specific quesionairre	X		9	2 minutes
Social determinents of health	CMS Health Related Social Needs	X		11	2-3 minutes
Spirituality	FACIT-SP	X	X	12	2-3 minutes
Fear of cancer recurrence*	Fear of Cancer Recurrence Inventory Short Form (FCRI-SF)[13]	X	X	12	2-3 minutes
Depression	Patient Health Questionnaire depression scale[14]	X	X	8	2 minutes
Anxiety	General Anxiety Disorder-7[15]	X	X	7	2 minutes
Resilience	Connor Davidson Resilience Scale -10 [16]	X	X	10	2-3 minutes
Post-traumatic growth	Post-Trumatic Growth Inventory[17]	X	X	21	3-4 minutes
Patient activation	Patient Activation Measure (PAM) [18]	X	X	13	2-3 minutes
Quality of life	PROMIS Global Short Form[19]	X	X	10	2-3 minutes
Life stressor question	Study Specific Survey	X	X	1	30 seconds
Acceptability	Acceptability of Intervention Measure (AIM) [20]		X	4	1-2 minutes
Appropriateness	Intervention Appropriateness Measure (IAM) [20]		X	4	1-2 minutes
Feasibility	Feasibility of Intervention Measure (FIM)[20]		X	4	1-2 minutes

*Only administered to patients with early stage breast cancer

3.7 *Compensation*: Participants who complete biomarker and survey portions of the study will receive a $50 gift card upon completion. Patients who complete the interview will receive an additional $50 upon completion ($100 total for Cohort 1, $50 for Cohort 2).

3.8 *Quantitative Analysis:* Cohorts will be analyzed both separately and together. The primary outcome is feasibility, which will be defined as 70% of women completing all intervention components and 70% of survey time points (baseline, post-surgery, post intervention)

being completed. Secondary endpoints will include implementation outcome measures by Weiner, which will evaluate the acceptability, appropriateness, and feasibility (survey-based) of interventions.[20] Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) are implementation measures with four-items each, and a response scale ranging from 1 to 5 (1 = Completely disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree, 5 = Completely agree).[20] Scores for each measure are calculated by averaging responses.[20] An average of 4 or greater on each measure (AIM, IAM, FIM) will be considered acceptable, appropriate, and/or feasible.

We will also capture the following measures for future comparative efficacy trial:

- **Fear of recurrence** will be measured using the Fear of Cancer Recurrence Inventory Short Term (FCRI_SF) which is scored from 0 to 4 (0 = Not at all, 1 = A little, 2 = Somewhat, 3 = A lot, 4 = A great deal)[13].
- **Patient depression** will be measured using the Patient Health Questionnaire depression scale[14], which is a 2 questions screener with 6 addional questions for an 8 question scale with a cut-point of greater than or equal to 10 being defined as current depression.
- **Patient anxiety** will be measured using the General Anxiety Disorder-7 scale,[15] which is a 7 item scale with scores of 0-4 signifying minimal anxiety, 5-9 mild anxiety, 10-14 moderate anxiety, and greater than 15 severe anxiety.
- **Resilience** using the Connor-Davidson Resilience scale which has 10 items each carry a 5 point range (0 = Not true at all, 1 = Rarely true, 2 = Sometimes true, 3 = Often true, and 4 = True nearly all of the time; total scores range from 0-40, and higher score indicate higher resilience)[16]
- **Post-traumatic growth** will be measured using the Post-Traumatic Growth Inventory (PTGI), which is a 21 item questionnaire with each item scored from 0-5 with 5 being greater degree of change.[17]
- **Social determinants of health** will be measured using the CMS Health Related Social Needs, which is a 11 question survey.
- **Spirituality** will be measured using the FACIT-SP is 12 question instrument.
- **Patient activation** using the Patient Activation Measure scores of which range from 0 to 100 with four corresponding levels [level 1 (0.0 - 47.0), level 2 (47.1 – 55.1), level 3 (55.2 – 72.4), and level 4 (72.5 – 100) which indicates the highest level of activation][18];
- **Quality of life** using the PROMIS Global Scale which is a 10-item measure that is scored from 1 to 5 (1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always).[19] (Table 2)
- **Recent life stressors:** We will use a single open-ended questions asking “Have you had any additional life stressors in the last 3 months (in addition to your breast cancer diagnosis and treatment)?”

Descriptive survey statistics will be calculated using frequencies and percentages for categorical variables and medians and interquartile ranges for continuous variables. Data will be analyzed in aggregate, by race, by residence in high vs. low resource census blocks, and by presence of dependent children in the home. Pre-post changes in survey scores will be examined using mixed models repeated measures analysis with two points of data capture: surveys capturing data at baseline (T_1) and after PRISM intervention (T_2). Linear contrasts will be used to estimate average change in survey scores between timepoints and compute 95% confidence intervals. The modeling approach uses all available data. Patterns of missing data will be examined and if necessary, models will be

adjusted with covariates associated with missingness. Normality of residuals will be examined, and if found to be non-normal, generalized linear modeling will be used.

No formal power calculation is needed for this pilot study as feasibility is defined by patient participation and completion of surveys. Following NIH guidelines, no formal testing will be conducted. Uncertainty of pre-post change estimates will be measured with 95% confidence intervals. Assuming 70% completion in the full sample (N=40), a standardized outcome, and intra-subject correlation values 0.5, 0.6, and 0.7, the upperbound half-widths of 95% confidence intervals for pre-post change are 0.38, 0.35, and 0.30, respectively. These provide reasonable ranges for potential values of change that can be expected in a future project (computations in PASS 23 software).

3.9 *Biomarker evaluation:* Data from biomarkers and ePROs will be merged with demographic data data using a study ID and date of collection. We will assess the relationship between biomarker outcomes and patient-reported outcomes. We will assess for correlational trends that would support evaluation in a larger cohort. We will examine distribution and ranges of biomarker data and determine whether variance stabilizing transformations are needed such as a natural logarithm, prior to analysis. As described above, we will employ a similar quantitative approach to compare pre/post intervention differences in assessed levels of cortisol, allostatic load, DAMPs and inflammatory response biomarkers (cytokines).

3.10 *Data linkage:* Both ePRO data and the data from biospecimens will be labeled using a Study ID. A separate tracking log will be kept with Study ID and MRN at UAB. This tracking log will be used to link datasets for analytic purposes.

3.11 *Qualitative Analysis*: The analytic strategy is informed by content analysis, which classifies text into categories that represent key concepts.[21] In the initial stages of coding, two independent coders will read the transcripts and develop an open coding scheme.[22] This initial coding scheme will consider the complexities of the lived experience of women with breast cancer, with particular emphasis on the wide range of factors that contribute to their experience of recurrence and generalized stress in their daily lives. The intention here is to construct a grounded, emic measure of vulnerability that can be directly compared to outcome variables within the study and accurately identifies areas within the PRISM intervention that require adjustment for this population. Analytic codes constructed in the context of open coding are provisional and will be grounded within the data.[23] The final version of the coding schema will be reviewed and finalized by the multidisciplinary team, which will include the interviewer, two primary coders, and the study PI, all having experience in oncology, anthropology, and/or implementation science. The two primary coders will subsequently use Dedoose to conduct “focused coding,” which includes a detailed analysis of themes identified during open coding. Discrepancies will be resolved by a third coder. The process will be repeated until thematic saturation is reached, where no new categories or relevant themes emerge.[24] Data will be analyzed in aggregate, by race, by residence in low resource areas, and by presence of dependent children in the home. During coding, we will consult regularly with the research team for multiple perspectives and discrepancy resolution through consensus. The coders will also code 20% of the transcripts to evaluate interrater reliability using a kappa statistic. If the kappa statistic is <0.7, the coders will discuss discrepancies, refine the code book, and complete another 20% of transcripts until the

kappa reaches 0.7.[25] Summaries will be reviewed with the research team and key partners for the future R01 to plan for next steps in the research.

3.12 *Sample size considerations:* Using a sample of 30 patients for breast cancer (10 MBC, 30 EBC) will provide initial data on feasibility, while larger studies will be needed for formally testing outcomes. Sampling for qualitative inquiries is sequential and targeted to individuals who can provide insights on the processes under study. Typically, qualitative approaches require <30 participants to reach thematic saturation. If thematic saturation is not reached, we will engage additional participants in the intervention and continue interviews until thematic saturation is reached.

3.13 *Mixed methods analysis*: We will validate our findings using both quantitative and qualitative methodologies that will be analyzed independently through side-by-side comparisons and thoroughly integrated using grounded measures derived from the interviews themselves. This mixed methodology will ensure that study findings are grounded in the appropriate context and will provide a comprehensive view of both study feasibility and necessary adaptations prior to conducting a future comparative efficacy trial.

4 Dissemination: We will utilize the descriptive data from the biomarker and patient-reported outcomes evaluation in combination with existing literature to generate a lecture for patients and physicians on stress in breast cancer.

5. Data and Safety Monitoring

Access to patient data will be limited to the medical care teams and relevant study staff. Data will be de-identified when possible and encrypted to enhance security. Data files sent between members of the research team will be de-identified. When unique patient identifiers (unrelated to any patient characteristics) are required to track patient-level outcomes, the files will be sent via secure transfer and stored on secure encrypted network drives. All qualitative data from participant interviews will be de-identified and securely stored on password-protected, encrypted network drives.

Multiple measures will be taken to ensure that the use of structured electronic medical record (EMR) data and manually abstracted EMR data involves the highest security precautions so that risks to individuals are limited. The data storage facility is located in a building with 24-hour security. The computers and data files are only accessible via a private gigabit-speed local area network to which only research team and clinical staff are connected. No routine traffic (e-mail, web, or other non-study services) travels on this network. All data are transmitted to investigators' workstations in an encrypted state. Only members of the research team and clinical staff will have access to identifiable data. All research team members will be trained in data security. All quantitative analyses reported from this study will contain only aggregate data. The qualitative data (e.g. quotes) from individual participants will be anonymously reported. The quality of the data will be monitored on a regular basis by members of the research team under the supervision of the Principal Investigator (Rocque) and statistician.

6. Benefits

Study participants may benefit from the intervention by improving resilience and psychological distress not only as it relates to their fear of cancer recurrence but skills learned in this intervention can be applied to multiple areas of their lives. Our findings could

benefit future patients with cancer by equipping patients with the knowledge and skills to improve stress management, resilience, and engagement with health care team.

7. Risks

Participants will not receive any pharmacologic treatment as part of this study, minimizing physical risks. This project will make use of health and other personal information about the study participants. The primary risk to the participants will be loss of confidentiality leading to potential psychological, financial, or legal consequences. However, using the data access and protection plan described above, we believe that the likelihood of confidentiality breach is very low. An additional risk that some PRISM sessions explore stressors, in turn prompting additional awareness of stress and corresponding distress. All coaches are trained in distress-recognition and suicide prevention; in >500 PRISM deliveries, there has been a single participant who endorsed significant distress prompting immediate coach intervention and referral (see Appendix Manual for procedures). In any case where coaches are concerned about participant distress, they will immediately contact the PI and the on-call social worker. In our experience, stress and distress during the sessions is short-lived and self-limited. Finally, there may be risk of discomfort from blood draws, although these will be completed in conjuction where possible with routine lab evalautions to prevent the need for additional venupuncture.

8. Confidentiality

Patients included in this study will be adult women receiving cancer care at UAB. The major risk for the study will be the risk of breach of data confidentiality. This will be minimized as described above in the data and safety monitoring section.

9. Clinical Trial Registration*:*

- Following initial IRB approval, this trial will be registered on ClinicalTrials.gov. All protocol revisions and estimated timelines will be reported within the system immediately following Institutional Review Board (IRB) approval.
- Results information will be submitted to ClinicalTrials.gov as outlined in the website's policy and according to the specific timelines stated therein.
- Informed consent documents for the clinical trial(s) will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov.

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