Protocol

1. **Project Title:** A Pilot Feasibility Study of a Gratitude Journaling Intervention to enhance Well-being and Exercise Readiness in Older African American Female Breast Cancer Survivors

2. **Investigator(s)**: Lakeshia Cousin, Ph.D., APRN

3. **Abstract**:

Complex comorbidities among older female survivors of breast cancer (BC) lead to increased symptom burden and postdiagnosis health care costs of at least $1 billion.[1-3] For older African American (AA) women, the burden of BC is even greater, with a 41% higher mortality rate and worse outcomes across all stages of BC compared to those of other racial/ethnic groups. The higher prevalence of obesity, metabolic syndrome, and triple-negative breast cancer (TNBC) among AA women contributes to these disparities.[4,5] Another contributing factor is the cultural phenomenon of the superwoman schema,[6] in which AA women feel obligated to manifest strength and suppress emotions while caring for others ahead of themselves. Within the socio-cultural and historical context of this schema, women may relegate actions to promote their own health secondary to caregiving, leading to higher levels of stress, obesity, and metabolic risk.[6-8] Research suggests that physical activity can attenuate metabolic risk factors, decrease BC mortality by 34%, and reduce race-based disparities in BC outcomes.[9,10] In the proposed study, we will assess the feasibility of a culturally tailored gratitude intervention designed to enhance psychological well-being and exercise readiness among female AA BC survivors.

Dispositional gratitude, defined as an appreciation of the positive aspects of life, is associated with better physical health among older adults.[11] Research has shown that practicing gratitude can positively impact levels of inflammatory biomarkers and individuals who practice gratitude are more likely to engage in more moderate-vigorous exercise.[12-18] The design of the proposed 8-week gratitude journaling intervention is based on the broaden-and-build theory of positive emotions,[19] which posits that dispositional gratitude serves to broaden people's thought-action repertoire, leading them to build physical and physiological resources that improve long-term well-being.[20] The intervention will also include a goal-setting component to promote exercise readiness and examine the Superwoman schema. Similarly adapted psychological interventions have led to improved physical activity in patients with cardiovascular disease.[21,22] Among majority-European American BC survivors, gratitude is associated with reduced psychological distress and enhanced spiritual well-being.[23-26] A significant gap remains, however, in the knowledge of the mechanisms underlying gratitude's link with physical health—especially its association with physical activity and inflammatory biomarkers in older AA BC survivors, who are at the highest risk of mortality and morbidity. Examining the preliminary feasibility and efficacy of a culturally tailored intervention to improve well-being and exercise readiness among female AA BC survivors is a critical first step toward the design and funding of a larger randomized controlled trial to test the effects of the intervention on biobehavioral outcomes.

4. **Background**:

Women aged 65 years and older account for more than half of the 3.8 million women living in the U.S. with breast cancer (BC).[5] Almost 30,000 deaths among women 60 years and older are attributed to BC, accounting for approximately 70% of all deaths from BC in the U.S. In addition to those 30,000 deaths, half of older women with BC die from causes related to comorbidities before and after cancer treatment.[1] Older BC survivors experience comorbidities and secondary malignancies, including cardiovascular disease and obesity. Metabolic syndrome, a set of biological factors linked to risk for cardiovascular disease and Type 2 diabetes (i.e., obesity, heightened inflammatory activation, hypertension, dyslipidemia, and dysglycemia), has been associated with an increased risk for developing BC with a worse prognosis and poorer outcomes. Recent studies have shown that AA women are 20% more likely to have metabolic syndrome than non-Hispanic European American women, and metabolic syndrome is the leading cause of racial/ethnic disparities in BC prognosis in the U.S.[27,28]

Significance. AA BC survivors may experience a higher level of stress from life events than BC survivors from other racial groups due to the superwoman schema, a set of cultural norms that encourages silence around psychological distress and the prioritizing of care for others over care for self. This increased stress leads to weight gain, inflammation, and a higher risk of metabolic syndrome.[6-8] These women are also at increased risk for obesity, which promotes inflammation, leading to increased levels of inflammatory markers.[10] Research

suggests that physical activity and a healthy diet can potentially attenuate metabolic risk factors, reduce BC mortality by 34%, and help reduce health disparities experienced by AA women.[10,29] AA women with BC can thus benefit from treatment plans that balance curative BC treatment with interventions that help prevent cardiovascular events and reduce related mortality. A growing body of evidence suggests that interventions utilizing mind-body techniques can help to improve inflammation, cell-mediated immunity, and biological aging as well as improve health behaviors, which can lead to longer-term improvements in health.[16,30,31] One potential therapeutic target for mind-body interventions targeting obesity and metabolic risk is growth differentiation factor 15 (GDF15), a stress-responsive cytokine associated with obesity, inflammation, cancer, metabolic diseases, aging, stressors, and the AA race.[27-31]

Dispositional gratitude, the tendency to appreciate the positive aspects of life, is strongly associated with increased spiritual well-being, lowered psychological distress, and improved health behaviors.[17,32-35] According to the broaden-and-build theory, gratitude can also influence self-efficacy.[15,16,19] The theory suggests that gratitude broadens an individual's repertoire of thoughts, actions, and attention, contributing to the building of physical and psychological resources over the long term. Our proposed intervention combines the practice of gratitude with that of goal-setting, which, according to Celano et al., can further increase adherence to health behaviors (see Figure 1).[36] Prior cardiovascular health studies have found that interventions pairing the use of optimism and gratitude with education and systematic goal-setting related to physical activity led to more physical activity, fewer hospital readmissions, and improved levels of inflammatory biomarkers.[21,36,37] *However, no similar studies have been performed in cancer patient populations.*

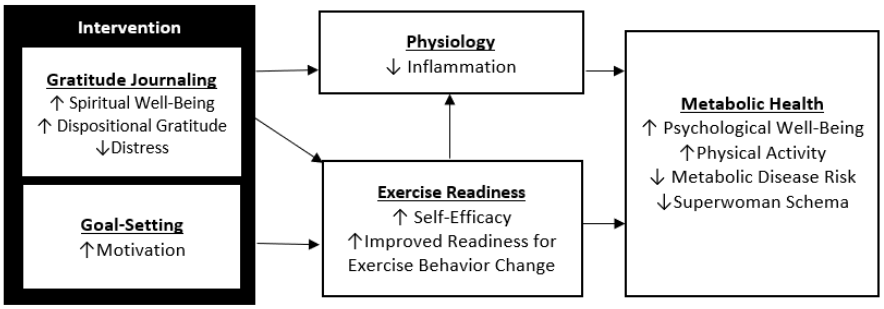

Figure 1: Theoretical Framework for a Combined Gratitude and Goal-setting Intervention

Innovation. We will test the feasibility and preliminary efficacy of a gratitude journaling intervention in older AA women with BC. Prior studies have deemed a similar intervention effective for majority-European American BC survivors, but no studies have explored its efficacy among AA women. *The proposed study will serve as the basis for a future randomized controlled trial to test the efficacy of gratitude journaling as part of a multimodal intervention to promote mental and physical well-being in AA BC survivors. The culturally targeted inclusion of the superwoman schema is an important theoretical innovation.*

Gratitude and Inflammatory/Aging/Senescence Biomarkers. As shown in Figure 2, the principal investigator's (PI) prior work provided evidence through a state of the science review to support the physical health benefits of gratitude among the general population and patients living with chronic disease. In our team's state-of-the-science review to explore the effects of gratitude on cardiovascular health outcomes among our sample of primarily European American men (*N* = 13), we found that most gratitude studies (*n* = 8) focused on improving biomarkers of health including markers of inflammation (C-reactive protein [CRP], interleukin-6 [IL-6], tumor necrosis factor-alpha [TNF-α], and soluble tumor necrosis factor receptor 1 [sTNFr1]), blood pressure, heart rate variability and hemoglobin A1C.[16] Individuals who practiced gratitude displayed improved inflammatory biomarker index scores, decreased diastolic blood pressure, lower heart rate, and reduced levels of hemoglobin A1C.[16] Although most studies suggested that gratitude had minimal effects on inflammatory biomarkers, some evidence showed promise. In a randomized controlled trial of older patients (*N* = 70), gratitude journaling improved dispositional gratitude scores and reduced inflammatory biomarker index scores over time and enhanced heart rate variability compared to a control group. Lacking from the literature are studies with diverse samples using culturally tailored gratitude interventions to promote ideal health behaviors. In our review, we also found emerging evidence that GDF15, a stress-responsive cytokine, has a role in regulating inflammatory pathways and that its biological processes are observed in cardiovascular disease and cancer.[38,39] Recent studies have suggested that increased serum GDF15 from lifestyle intervention is associated with metabolic improvements among obese adults.[38-40] These findings support the use of GDF15 as an indicator of metabolic improvements in studies testing interventions such as that proposed here.

Associations of Gratitude with Physical Health. The link between gratitude and physical health is associated with increased psychological well-being and adherence to recommended health behaviors, which, in turn, lead to better physical health across adulthood.[11] Psychological factors such as gratitude and educational interventions can help improve treatment adherence in other clinical populations such as individuals with cardiovascular disease.[21,22,37] In an earlier study, the PI developed and tested a structural equation model of the relationships between gratitude, self-efficacy and medication adherence in heart failure patients and found that self-efficacy was a mechanism through which gratitude was associated with medication adherence.[15] In a recent study among the general population (*N* = 4,825), gratitude was associated with less stress, greater appreciation, lower heart rate and blood pressure, and greater participation in moderate and vigorous exercise.[18] Gratitude studies in patients with BC have, to this point, focused mainly on facilitating psychological and spiritual well-being.[23,25,26,41,42]

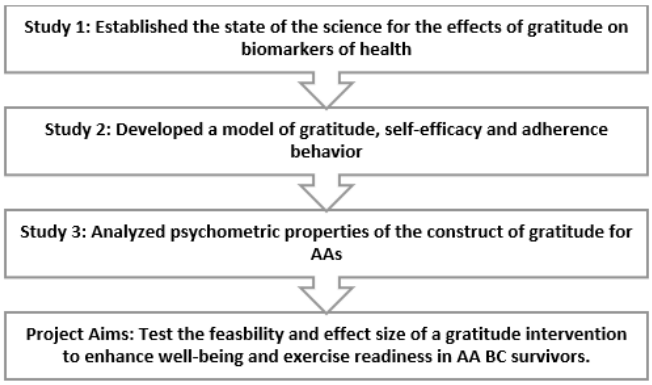

Figure 2. Preliminary Studies by Lead Investigator

Cultural Context: Gratitude and Spiritual Well-Being in African Americans. Historically, AA women have used spirituality to inspire hope when dealing with hardships.[43-45] Among AA BC survivors, spiritual well-being is a primary coping mechanism during all phases of treatment and survivorship. Contextual factors associated with a higher degree of spirituality include self-efficacy, collectivism, and Afrocentric worldviews.[46] Gratitude and spiritual well-being have both been related to improved mood, higher rates of self-efficacy, and lower levels of inflammatory biomarkers in other clinical populations.[17] The PI was the first to successfully assess the characteristics of the Gratitude Questionnaire-6 (dispositional gratitude) in AAs at risk for cardiovascular disease (*n* = 298).[47] Findings indicated that dispositional gratitude was positively correlated with positive affect and spiritual well-being and negatively correlated with depressive symptoms. The PI's future work will examine whether these contextual factors influence physical health outcomes in AA women.

5. **Specific Aims**:

My *long-term goal* is to reduce morbidity and mortality risk in older AA BC survivors by developing culturally tailored interventions to improve health outcomes and behaviors. In this application, our *overall objective* is to assess the feasibility of a gratitude intervention to promote physical activity and positively impact inflammatory biomarkers to reduce metabolic risk.

Aim 1. Assess the feasibility and acceptability of a gratitude journaling intervention using a pilot randomized controlled trial (RCT) two-group parallel design over eight weeks. We *hypothesize* that among the 28 participants 1) at least 80% of the participants in both arms will report the study to be acceptable, 2) biomarker collection will be completed in at least 80% of the surveys and the retention rate will be 80% in each group, and 3) physical activity, health markers, gratitude, well-being, and distress will improve over time in the gratitude intervention group than those in the attention control group.

Aim 2. Describe differences and distributions of outcome variables and effect size for the gratitude journaling intervention compared to the attention control group on dispositional gratitude, spiritual well-being, psychological distress, exercise readiness, mental and health behaviors in AA women (Superwoman Schema), and inflammatory biomarkers from baseline to post-intervention.

Research Plan:

We will conduct a pilot feasibility study for the gratitude intervention using a two-group parallel random-assignment experimental design to achieve our aims. We will use resources from the Clinical Research, Metabolism and Translational Science, and Biostatistics Cores of the UF Older Americans Independence Center's (OAIC) / UF Clinical and Translational Science Institute (CTSI) to conduct this study.

Study Participants: As per the recommendation of Julious[48] for 14 participants per group for a pilot study due to no prior information to base a sample size, we will recruit 28 participants for this two-group study to account for a potential attrition rate of 10%. We will recruit AA women from all socioeconomic groups with a history of BC

treated with chemotherapy using organic social media recruitment, flyers ,multiple specialized recruitment strategies from the OAIC Clinical Research Core - Claude D. Pepper Center Participant Registry (IRB201601352), UF Health Cancer Center Community-Partnered Cancer Disparities Research Collaborative (CDRC), UF Health Cancer Center Community Outreach and Engagement, UF Healthstreet, Integrated Data Repsitory and UF Consent2Share Registries. Potential participants will be screened for eligibility via telephone. Eligible participants will be English-speaking, self-reported AA/Black, postmenopausal women with a history of BC (Stage I–IV) who are 3 months to 6 years post-adjuvant chemotherapy. Women on hormonal therapies and anti-human epithelial receptor 2 (HER-2) therapy will be included. Exclusion criteria include self-reported regular meditation or gratitude practices (more than once a week for at least a month) or currently meeting the Centers for Disease Control and Prevention (CDC)'s physical activity guidelines. Women will be compensated $100 within two time points for their participation.

Study Design: We will adhere to intervention fidelity using the five standard NIH recommendations for intervention fidelity: 1) design of the study; 2) intervener training; 3) treatment delivery; 4) treatment receipt; and 5) treatment enactment.

NIH Recommendations	Description of Treatment Fidelity (Both Arms)
Design of study	To reduce variability in outcome measurement, we will train our research assistant and research intern using a detailed intervention manual to instruct the participants on how to provide journaling education. The interventional manual will include detail on how to use the journal prompts specific to the treatment group (gratitude) and control group (general memories). The prompts are included in a custom-designed journal (i.e., a gratitude-specific journal and a general memory journal) with dates and prompt listed inside each journal. The journal will include 1-2 major physical activity goal page, and an exercise educational resource to promote exercise readiness and self-efficacy. Additional forms to be used for data collection will be appropriately designed to encourage the collection of good quality data. They will be user-friendly, self-explanatory, and clearly formatted. The PI and study staff will provide any technical assistance regarding journaling for the participants and a direct number and email address for any additional issues that may potentially arise.
Intervener Training	Because all training content explained at baseline is uniform, and the journaling will be recorded in the journals at least twice a week, there will be no deviance in the provision of the program across participants.
Treatment Delivery & Receipt	A study-specific protocol will be developed and explicitly followed. Dosing (times per week the participant completed journals and practice) will be meticulously tracked by evaluating: the number of journal entries at least twice a week and the number of words written per journal entry in the hardcover journal. The journal will be given at week 0, and the journal will be collected after week 8 during the final appointment. We will limit the entries to six memories, with a target goal of 10-15 minutes spent journaling, and no set schedule (having entries occur in the morning or evening). The study staff will provide a weekly email reminder to enter a journal entry at least twice a week.
Treatment Enactment	We will follow participants from week 0 to week 8 to determine sustained use of the intervention (intermediate output).

Gratitude Intervention: The proposed study builds on Emmons and McCullough's original gratitude journaling intervention.[49] The original intervention, mostly undergraduate psychology students, did not include a goal-setting exercise and conducted daily gratitude journaling. However, prior cardiovascular health studies have found that interventions pairing optimism and gratitude with education and systematic goal-setting related to physical activity led to more physical activity, fewer hospital readmissions, and improved levels of inflammatory

biomarkers.[36] Therefore, this study will pair the use of goal setting and physical activity education and to reduce the burden of journaling for cancer survivors and the participants will journal at least twice a week. During the initial session, the Principal Investigator or research assistant will provide a journal kit and an educational physical activity brochure to assist in setting 1-2 physical activity goals during the study period.

For the gratitude intervention, each participant will receive a gratitude journal for the eight-week period and will have the following journaling prompt to complete for at least twice a week for a duration of 10-15 minutes: "There are many things in our lives, both large and small, that we might be grateful about. Think back over the day and write down on the line below all that you are grateful for today" (maximum six reasons). The educational component on goal setting will drawn from the American Cancer Society's *Nutrition*, *Physical Activity, and Cancer* toolkit. Participants will be able to choose the order in which they complete the goal-setting modules. Both of these exercises will be administered at least twice a week over 8 weeks, preferably at the same time each day with a target goal of 10-15 minutes. Each participant will have the option to complete either a paperback journal or an electronic journal via Qualtrics.

For the attention control arm, participants will receive a receive the following general journaling prompt for at least twice a week for no more than 15 minutes: "What are some memorable events that happened to you today, big or small (maximum six memories). Write a brief statement about it. At the end of the intervention, at week 8, we will collect the journal for treatment fidelity. We will give the option to mail the journal back to the participant as a keepsake if requested.

Data Collection and Study Procedures: After screening for eligibility and collection of verbal consent, we will schedule an in-person appointment to collect baseline data, including collection of a blood sample (see Table 1 for measures and variables to be collected). Before the appointment, we will send demographic and cancer history questionnaires and self-report instruments (listed below) to participants for review. Informed written consent will be obtained at the in-person appointment, and an electronic survey will be sent following completion of the first appointment. After baseline (T1) data collection, participants will be randomized to either the gratitude journaling intervention or attention control group in a 1:1 ratio using online randomization software (http://randomization.com), and block randomization to ensure equal distribution between groups. The PI will inform participants of their group assignment and provide intervention details. The research assistant and biostatistician will be blind to group allocation. Participants will begin their daily intervention within 1 week of completing T1 data collection. They will also be scheduled for their T2 data collection appointment, which will occur 8 weeks after the start of the intervention and will include the same measures as baseline excluding the demographic and cancer history questionnaires. Data will be stored in Qualtrics on a secure university server and password protected with the assistance of the Biostatistics Core.

Blood Collection, Processing, and Storage: Blood samples will be obtained by a registered nurse or phlebotomist using the CTSI's standard protocol at the UF Clinical Research Center. After a ten-minute rest period, up to 10 ml of blood will be drawn. No more than two attempts will made to obtain blood samples with any participant. Blood samples will be collected, processed and stored with the OAIC Metabolism and Translational Science Core in the UF Clinical Research Center.

Table 1. *Study Measures.*

Outcome (Time Points)	Measure/Description
Demographics (T1)	Age, sex, education, marital status, body mass index; cancer- and treatment-related variables including time since diagnosis, cancer stage, grade and other disease-related variables including hormonal and HER2 status, surgical type, chemotherapy, radiotherapy, and cancer treatment.
Dispositional gratitude (T1, T2)	The Gratitude Questionnaire-6 (GQ-6), a well-validated, self-administered 6-item scale, is designed to measure four facets of dispositional gratitude:[49] (a) intensity, (b) frequency, (c) span and (d) density. Each item is rated on a 7-point Likert-type scale ranging from 1 (strongly disagree) to 7 (strongly agree).
Spiritual Well-Being (T1, T2)	The Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being 12 Item Scale (FACITsp12) is a 12-item scale designed to assess spiritual well-being over the past 7 days in a population with a chronic illness.[50] Items are rated on a Likert-type scale ranging from 0 (not at all) to 4 (very much).
Distress (T1, T2)	The Perceived Stress Scale (PSS), used to measure stress, consists of 10 items rated on a 5-point Likert scale ranging from 0 (never) to 4 (very often) during the last month.

Outcome (Time Points)	Measure/Description
Superwoman schema (racial and gender identity) (T1, T2)	The Giscombe Superwoman Schema Questionnaire (G-SWS-Q) was developed to measure components prominent in the superwoman schema construct.[6,51] It contains 35 statements rated from 0 (not true) to 4 (true all the time) across the 5 subscales of (1) obligation to present an image of strength, (2) obligation to suppress emotions, (3) resistance to being vulnerable, (4) intense motivation to succeed and (5) obligation to help others. Higher scores indicate higher agreement with the identity.
Exercise readiness (self-efficacy and stages of exercise behavior change) (T1, T2)	Exercise readiness will be assessed using the Stage of Motivational Readiness for Physical Activity questionnaire, a highly reliable instrument with 5 items that classify a person as being in the pre-contemplation, contemplation, preparation, action, or maintenance stage of exercise behavior change.[52]
TNF-α, IL-6, GDF15 (T1, T2)	Luminex panel
CRP (T1, T2)	Enzyme-linked immunosorbent assay (ELISA) kit
Treatment satisfaction (T2)	The Client Satisfaction Questionnaire (CSQ) is a standard measure used across health care delivery and will be used to assess the acceptability of the gratitude intervention.[53]

Feasibility Outcomes: The number of potential participants screened and enrolled will be tracked to evaluate recruitment and retention rates for the study. Participant adherence to the intervention will be calculated based on the journal logs. Exit interviews and the CSQ will be administered at T2 to evaluate the intervention's usability and usefulness and participant satisfaction with the study. The exit interview will comprise both structured and open-ended questions about the participants' perception of the intervention's content, value, structure, and potential burden.

Inflammation and Aging/Senescence Biomarkers: Following collection of the blood sample, the plasma will be separated, aliquoted, and stored at −80°C for later assay. A custom multiplex immunoassay panel for TNF-α, IL-6, and GDF15 (R&D Systems, Minneapolis, MN) will be analyzed using a MILLIPLEX® Analyzer 4.3 xPONENT System (Luminex Corp, Austin, TX). CRP will be measured via ELISA (R&D Systems) using a BioTek Instruments (Winooski, VT) Synergy™ HTX Multi-Mode Microplate Reader and analyzed via Gen5 Microplate Reader Software (Bio-Tek Instruments). Analyses have a minimal interassay coefficient of variation < 14.

Data Analysis

Distributions, including missing-data patterns and the presence of out-of-range values for all variables, will be examined using descriptive statistics appropriate for level of measurement. We will assess participant satisfaction using mean CSQ scores and exit interview questions. The CSQ will provide additional details regarding the gratitude and goal setting exercises, which will be used as an indicator of demand (criterion: > 80% of participants enrolled) and correlated with measures provided. Feasibility will be measured by the proportion of women who meet the inclusion criteria relative to the number of women approached (feasibility defined as > 75% women approached meeting criteria), percentage of participants completing baseline assessment measures (feasibility defined as > 80% of participants completing measures), and percentage of participants who complete baseline assessments completing post-intervention assessment (feasibility defined as > 80% of those who complete baseline assessments completing post-intervention assessments).

Separate two-by-two mixed-effects general linear models (GLMM),[54] comprised of effects for treatment, time, and treatment-by-time interaction, will be used to estimate effect sizes for each of the outcome variables. The distribution of residuals will be evaluated for the tenability of model assumptions, and, where necessary, remedial measures such as Box-Cox transformations will be applied. CONSORT guidelines for intent-to-treat principles will be used for hypothesis testing to manage missing data related to attrition. We will determine differences between groups using t-tests.

6. **Possible Discomforts and Risks**:

Protection of Human Subjects

According to federal regulations and NIH policy, applications that propose to involve human subjects must address risks to human subjects (human subject characteristics, involvement and design; sources of materials; and potential risk); adequacy of protection against risks (recruitment and informed consent and

protections against risk); potential benefits of the proposed research (are potential risks to subjects reasonable in light of anticipated benefits?); the importance of the knowledge to be gained; and a data- and safety-monitoring plan/board. We address each of these requirements below.

Risks to Human Participants

Inclusion/Exclusion Criteria. Table 2 lists study inclusion/exclusion criteria. Exclusion criteria are designed to prevent inclusion of participants who would experience discomfort or harm during collection of blood or other data and to protect the data integrity of the participants.

Table 2. Inclusion and Exclusion Criteria.
Inclusion Criteria • Self-report as AA or Black • English speaking • History of BC (Stage I–IV); 3 months to 6 years post-adjuvant chemotherapy • Participants on hormonal therapies or HER-2 therapy are acceptable
Exclusion Criteria • Self-reported regular meditation or gratitude practices (more than once a week for at least a month) • Meeting the CDC's physical activity guidelines (at least 150 min of moderate-intensity aerobic physical activity or 75 min of vigorous-intensity physical activity, or an equivalent combination each week)

Blood-draw collection. Although generally safe, blood-draw collection procedures can confer limited risks, including that a participant will experience pain or discomfort. To minimize discomfort, we will make no more than two attempts per time point to obtain blood samples with any one participant.

Onsite adverse events. In the event of any of the following adverse events, we will immediately notify a physician and the IRB: 1) deaths, 2) falls, or 3) health events that result in immediate hospitalization or medical care.

Attrition. Given the success of the studies conducted at the UF OAIC Clinical Research Core, we do not expect any recruitment issues. However, since this proposal requires two visits to the institute, we are anticipating 5%–10% attrition. We will thus gather all primary data (blood draw and electronic questionnaires) during the T1 visit. At the T2 visit, we will collect another blood draw and the electronic questionnaires and conduct exit interviews and administer the CSQ to evaluate usability, usefulness, and participant satisfaction. Both structured and open-ended questions will be used to assess participants' perception of the intervention's content, value, structure, and burden. To further minimize attrition, we will (1) educate participants during the initial telephone screening about the importance of committing to the study, (2) obtain complete contact information (including alternative email addresses and phone numbers), (3) place a reminder call and/or email (if available) 2 days before the scheduled visit, and (4) provide compensation upon completion of each visit.

Inadequate Sample Size. Since this is a pilot feasibility study, which requires a relatively small sample, it may be underpowered to detect statistically significant differences in outcome measures. However, it will provide the information necessary to design future adequately powered efficacy studies.

Adequacy of Protections Against Risks

The PI and research assistant will obtain informed consent, conduct participant screening, collect questionnaire data, monitor the experiment, implement the intervention, and ensure the safety of the participants. All procedures will be conducted by trained personnel. All persons responsible for the intervention will undergo thorough training. The laboratory is equipped with a telephone in case of an emergency, and in-house registered nurses (clinical research nurses) are also available. Emergency phone contacts will be posted in the laboratory's manual of operations, and all experimenters will be informed about who to contact in the event of emergencies. Participants will also be informed that multiple measures will be taken to ensure their safety. Participants may withdraw from the study at any time.

Description of Informed Consent. IRB approval will be obtained before participant recruitment begins. Potential participants will be administered a brief phone screening to assess their appropriateness for the study. During the call, they will receive a brief description of the study procedures, including information about the nature of the questionnaires and blood-draw collection and associated risks. If they agree to participate, the PI will review the details of the study with them and review the written informed consent in detail in a private research study exam room during the initial visit at T1. Women will participate in the study only after they provide verbal and written informed consent. The informed consent form will include standard information, including a description of the research protocol, the potential risks and benefits of participation, participant assurances, and contact information for the PI. Participants will also be informed that they can withdraw from the study at any time and that this will have no adverse impact on the study or their future medical treatment. Potential participants will be provided a copy of the informed consent form to review before being asked to sign. Informed consent will be documented via the participant's and investigator's signatures. A signed copy of the informed consent will be provided to participants during the initial visit.

Sources of Data. Data from questionnaires will be the primary sources of research material. General health information regarding significant medical conditions will also be collected. Questionnaire and experimental data will be used specifically for research purposes. Any hardcopies of the data will be stored in a locked cabinet in the PI's university office accessible only to her, saved for the length of time required by law, and then destroyed.

Research personnel. Trained and salaried personnel from the University of Florida College of Nursing and OAIC Clinical Research Core will assist with research procedures. Volunteers will receive training regarding the administration of questionnaires via a training session followed by observation a research staff member while s/he performs the consent process and standard study protocols and the volunteers' completion of two mock participant visits.

7. **Possible Benefits**:

Evaluation of Risk/Benefit Ratio. We believe that the expected benefits of participation outweigh the potential risks. Participants will benefit from exposure to the motivational techniques to promote gratitude, exercise readiness, and goal setting. We also hope that knowledge gained from the study will provide new information regarding culturally relevant factors that can improve metabolic health among AA BC survivors. Ultimately, such knowledge could enhance the well-being of AA cancer survivors.

Compensation. All procedures necessary for the completion of this study will be performed at no cost to the study subjects. Based on the amount of time and effort required for each visit, women will be eligible for a total of $100 for their study participation.

Importance of Knowledge to Be Gained

The findings from this study will have relevance to the fields of oncology, gerontology, and psychology. Older AA women experience disproportionately higher rates of mortality and other poor outcomes across all stages of BC due to the higher prevalence of obesity and metabolic syndrome in AA women. The data obtained from the current study will lead to the development of a model to identify the underlying mechanisms through which gratitude can influence physical-activity behaviors that will reduce risk factors for metabolic disease among AA BC survivors. The model will subsequently guide the development of a behavioral intervention to enhance inflammatory biomarkers and health-behavior adherence among AA BC survivors.

Data- and Safety-Monitoring Plan/Board (DSMB)

The PI and study team established a framework for the oversight and monitoring of this pilot feasibility study by the Claude D. Pepper Older Americans Independence Centers (OAICs) as an OAIC funded study. The PI will monitor study-related activities on a continual basis for compliance to the protocol. All personnel assisting with the study will be instructed on the importance of protecting participants' confidentiality. All research personnel (i.e., PI and volunteer RAs) will complete a series of annual trainings regarding human subject protections, HIPAA/confidentiality, protected health information, and protection of social security numbers. All paper and computer records will be identified by participant ID number rather than name. The list linking participant ID numbers to their identities will be maintained in a password-protected data file, accessible only by authorized research personnel associated with the human-subjects components of this project. All paper-based study records will be stored in locked file cabinets and will only be available to the PI or other project staff. Computer

data files (without subject identifiers) will be stored on computer servers with secure passwords, and electronic storage devices will be encrypted. Consent, and any other forms with identifiable subject information, will be maintained in a locked file separate from the actual study data files. Participant ID numbers will be used in all data tabulation and subsequent publication. We will be using a secure Web-based data-collection and -management system (i.e., Qualtrics, REDCap) that utilizes SSL-encrypted Web-based interfaces and enterprise-class database back ends. The University of Florida employs a site-wide monitored network. Thus, all electronic data will be maintained in a highly secure manner.

Adverse events and unexpected problems involving risks to subjects will be recorded on the online form "Serious and Unexpected Adverse Event and Safety Report" developed by the University of Florida's IRB. This form collects a description of the event, the course of action taken, and specification regarding whether the event was: 1) serious (e.g., requiring hospitalization, resulting in significant disability/incapacity or death); 2) unexpected, and 3) more than likely related to the study interventions/procedures. All serious and unexpected adverse events are to be reported to the University of Florida IRB within 5 working days and to the study's sponsor. Less-serious adverse events will be monitored and reported to the University of Florida's IRB in the study's annual progress review.

Inclusion of Women, Minorities and Children

Inclusion of Women. BC predominantly affects women; thus, only female participants will be recruited (*N* = 26).

Inclusion of Minorities. All participants will self-report as AA or Black women.

Inclusion of Children. Children will not be included in the proposed study as the focus of this application is to investigate mechanisms of gratitude, well-being, and exercise readiness associated with older adult survivors of BC.

8. **Conflict of Interest**: The principal investigator declares that there is no conflict of interest in conducting this study.

References

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