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DESIGNING WITH DISSEMINATION IN MIND: OPTIMIZATION OF A MHEALTH PHYSICAL ACTIVITY INTERVENTION FOR BREAST CANCER SURVIVORS (FIT2THRIVE STUDY)

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1.0 Objectives

1.1 Purpose and Specific Aims

Breast cancer survivors are at an increased risk of chronic conditions and compromised quality of life (QOL).[1,2] Increased physical activity (PA) is associated with reductions in negative treatment-related side effects (e.g. fatigue, depression), cancer recurrence and mortality and improved QOL and survival.[3-6] However, breast cancer survivors demonstrate decreases in PA that persist post-treatment,[7,8] and up to 70% do not meet public health recommendations for PA.[9-12] Although many factors[7,13-18] contribute to survivors' low PA, a lack of accessible, effective PA programs is a major barrier. Most existing PA interventions are resource-intensive, on-site programs tested in controlled efficacy trials with little chance of being translated into real-world practice.[19] Therefore, it is critically important to develop theoretically sound, cost-effective PA interventions that can be remotely delivered with greater dissemination and implementation (D&I) potential.[18-22]

Our previous prospective study indicates that social cognitive[23] constructs including self-efficacy, outcome expectations, social support and goal-setting may be useful targets for PA interventions among breast cancer survivors.[15] However, PA interventions targeting these constructs typically use bundled packages consisting of standardized doses of multiple components (i.e. daily logs, support calls, feedback) delivered simultaneously making it impossible to disentangle which intervention components, at what levels, and in what combination(s) do, or do not, impact target constructs and maximize PA. Granular information about the effects of discrete components is needed to optimize intervention configuration so PA and scalability are maximized and burden and cost minimized.[20,24] Using traditional study designs (i.e. randomized clinical trials) to test each component one at a time is inefficient in terms of time and expense. More efficient research methods must be used to simultaneously compare the effects of multiple individual intervention components.

The purpose of the present study is to apply the Multiphase Optimization Strategy (MOST)[25] to develop and pilot test a set of mobile health (mHealth) PA intervention components for breast cancer survivors that are targeted at social cognitive constructs known to impact PA uptake and designed with D&I in mind from the outset. MOST is an innovative multi-phase framework adapted from engineering that uses highly efficient factorial experiments to evaluate the individual and combined effect of intervention components. The present study will use a MOST approach to examine the effect of PA intervention components that vary on cost. These data will be used to assemble an intervention to be evaluated in a larger R01 that is optimized to yield the maximum increase in PA for the minimum cost. The proposed study represents the first systematic effort to use MOST to design a highly disseminable PA intervention for breast cancer survivors. The resulting intervention will have great potential for scalability because it engages relevant stakeholders (i.e. survivors, experts, community leaders) in the design, uses technology (smartphones) participants already own, requires no on-site visits, and recruits using the Army of Women,© a national breast cancer research registry the PI successfully used previously.

Specific Aims:

Aim #1. Use a patient-centered approach to select a set of five PA intervention components for breast cancer survivors designed to impact social cognitive constructs. Although we have identified candidate app/intervention components, selection of which ones to test will be made based on consensus between investigators and relevant stakeholders including survivors, experts and community leaders (n=10 of each). Survivors (n=10-20) will also be involved in iterative testing to determine app usability and functionality.

Aim #2. Pilot test the feasibility and acceptability of candidate intervention components in a 12-week MOST experiment. A highly efficient experimental design will be used for this pilot study of survivors (n=256). Feasibility will be assessed by a) intervention reach, b) participant retention, and c) adherence to the intervention protocol. Acceptability will be assessed by ratings of the acceptability and usefulness of intervention components.

Aim#3. Examine effects of the intervention components on PA. The effect of the intervention components on changes in accelerometer measured PA (minutes/week) at 12 weeks and 24 week follow-up will be examined using a highly efficient experimental strategy powered to detect effects of individual components.

Exploratory Aim. Examine potential effects of the intervention components on important patient-reported outcomes (PROs). We will examine the effect of each intervention component on changes in physical function, fatigue, depression and QOL at 12 weeks and 24 week follow-up using well-validated self-report measures.

Exploratory Aim 2. Examine the effects of the 5 intervention components on biomarkers of breast cancer (BC) progression and cardiovascular disease (CVD) risk in a 12 week intervention. We will collect blood samples for future research to examine evaluate the extent to which each intervention component ameliorates a pro-inflammatory phenotype associated with BC progression and CVD risk (i.e. interleukin-6, tumor necrosis factor-alpha interleukin-10, c-reactive protein) and cardiometabolic biomarkers (i.e. glucose, triglycerides, total cholesterol and high-density lipoproteins).

1.2 Hypotheses to be tested.

Aim #1. We hypothesize that a set of 5 components will emerge as favored by participants and approved by experts and investigators.

Aim #2. The primary hypotheses are: a) 75% of eligible survivors will agree to participate in the intervention; (b) enrollees will demonstrate engagement by monitoring PA on >80% of the study days and using one or more additional app components at least weekly. Descriptive analyses (means, frequencies) will be used to describe these results

Aim#3 and Exploratory Aim #1 and #2. Our hypothesis is that a set of components will emerge as most effective for increasing PA and minimizing cost but a additional

configurations of intervention component may emerge as having the largest, most cost-efficient impact on PROs, biomarkers of BC progression and CVD risk .

2.0 Background

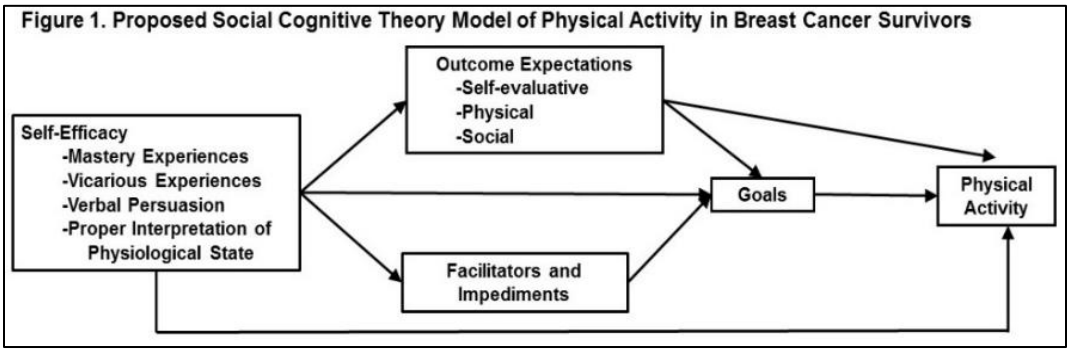
2.1 *Relevant Prior Experience and Gaps in Current Literature*

Breast Cancer Survivors and Physical Activity Overview. An estimated 3 million breast cancer survivors are alive in the U.S. with this number expected to increase to 4 million over the next decade.[26] Cancer and its treatment are associated with a host of deleterious psychosocial (e.g. fatigue, depression, low self-esteem) and physical side effects (e.g. nausea, vomiting, lymphedema, functional limitations) that may be chronic or have a late onset and result in compromised quality of life (QOL).[27] Breast cancer survivors are also at an increased risk of early mortality and the development of both comorbid conditions[28] and second primary cancers.[29] Increased physical activity (PA) has been shown to be effective for reducing these negative treatment-related side effects and improving QOL.[5,6] Increased PA is also associated with increased survival and reduced risk of recurrence, progression and all-cause mortality in this population.[30] Consequently, evidence-based guidelines recommend that breast cancer survivors engage in moderate to vigorous intensity aerobic PA for 150 minutes per week, with the benefits believed to be dose-dependent.[31,32]

Despite the benefits of PA, up to 70% of breast cancer survivors do not meet PA recommendations.[9-12] Although many factors[7,13-17] contribute to dismal PA levels, a lack of widely available disseminable evidence-based PA programs for breast cancer survivors may be a major barrier.[19] Most existing PA interventions for breast cancer survivors are on-site, intensive, professionally delivered multicomponent programs. The few home-based PA interventions involve a large number of face-to-face or phone counseling sessions and do not incorporate web or mobile technology. Historically, design of these time and resource intensive interventions has largely neglected to engage stakeholders (i.e. clinicians, survivors) and ignored contextual barriers (i.e. cost, burden, and accessibility) that influence real-world intervention uptake and sustainability.[19] Thus, existing PA interventions are often not feasible for widespread dissemination and implementation (D&I).[19] As the number of breast cancer survivors continues to increase, it is of critical public health importance to develop more disseminable, effective PA interventions to improve health and disease outcomes and reduce healthcare costs. The proposed study addresses this critical need by designing with D&I in mind from the outset by engaging stakeholders in intervention development, using mobile technology for intervention delivery to increase reach and accessibility, and identifying “active” intervention components.

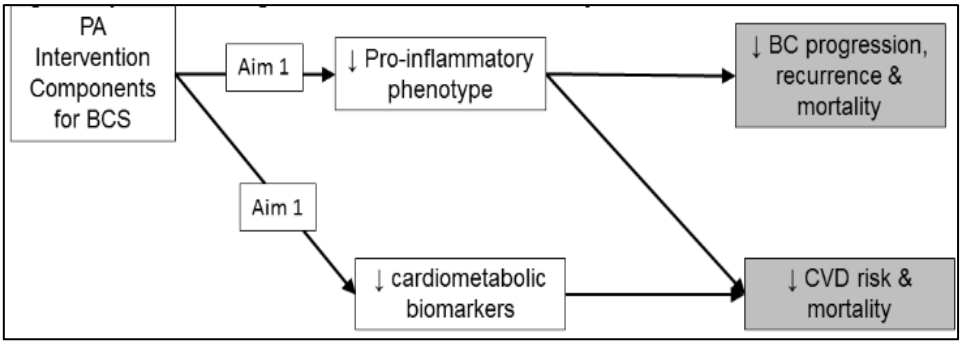
Social Cognitive Theory (SCT)[23] is well recognized as a useful framework for the design of PA interventions. However, the full model has been applied less-frequently in research with cancer survivors.[33] SCT[34-36] specifies a core set of determinants (self-efficacy, goal-setting, facilitators/barriers outcome expectations) and the mechanisms through which they work.[35] Specifically, individuals with higher self-efficacy have more positive outcome expectations, set higher goals, and are more likely to believe they are capable of overcoming barriers (see Figure 1). These relationships are all postulated to be reciprocal (i.e. higher self-efficacy is associated with higher outcome expectations and vice versa).

Our work, and the work of others, has demonstrated SCT constructs including self-efficacy, realistic outcome expectations, facilitators/barriers (i.e. social support), and goal-setting are associated with increased PA in breast cancer survivors.[15,37-39] Most PA interventions that use SCT involve simultaneous delivery of multiple intervention components (e.g. goal-setting activities, PA logs, social support) intended to target these constructs. While this approach results in determination of overall intervention effectiveness, it provides little insight into which intervention components/SCT constructs were, or were not, effective. Identifying which intervention components maximize PA while minimizing cost can help to determine which components should be included, eliminated or reduced to meet specific organization or individual needs.



Physical activity (PA), breast cancer (BC) prognosis, and cardiovascular disease (CVD) risk. Overall relative survival rates are high for breast cancer. However, BC survivors (BCS) are still at risk for recurrence and they demonstrate higher CVD incidence and mortality[40] than healthy controls. CVD is also the leading cause of non-cancer death among BCS.[41] Increased CVD risk in BCS likely results from a combination of treatment toxicities[42,43] and poor lifestyle habits.[44] Increasing PA may improve both BC progression[45] and reduce CVD risk[46] in BCS. A recent meta-analysis found that BCS who participated in the most PA post-diagnosis had a lower risk of BC-related death, death from any cause, BC progression, and new primary cancers and recurrence compared to inactive BCS. [45] Further, data from the general population indicate increased PA is associated with reduced CVD risk and mortality.[47,48] While these findings are promising, the exact biologic mechanisms underlying the benefits of PA on BC progression and CVD risk in BCS are not well-established.

Fig. 2 Proposed BC Progression and CVD Risk pathways to be Examined



PA and BC prognosis and CVD risk biomarkers. PA is hypothesized to improve BC progression via its effects on a number biobehavioral pathways, including inflammation.[49,50] A pro-inflammatory phenotype is associated with increased BC progression and mortality and CVD risk and mortality[51-54] while higher PA is associated with amelioration of a pro-inflammatory phenotype.[55] Higher PA may be associated with further CVD risk and mortality reductions in BCS via its effects on cardiometabolic biomarkers.[56] Figure 2 displays these pathways. The proposed study will contribute to the evidence needed to advance a public health-level recommendation that BCS should engage in PA. **Inflammatory biomarkers.** Interleukin-6 ***(IL-6)*** and tumor necrosis factor-alpha ***(TNFα)*** are pro-inflammatory cytokines secreted by tumor cells, infiltrating macrophages, and adipocytes. Preclinical studies suggest TNFα is associated with increased angiogenesis and invasion[57,58] and IL-6 promotes proliferation, inhibiting apoptosis and promoting conversion of noncancer cells into tumor stem cells.[59] Interleukin-10 ***(IL-10)*** is an anti-inflammatory immunosuppressive cytokine with both pro- (reduces antigen presentation, cell maturation and differentiation which may allow tumor cells to evade immune surveillance mechanisms)[60] and anti- (inhibits gene expression, cytokine synthesis by T cells and macrophages, and their antigen presentation)[61] tumoral effects.[62] C-reactive protein ***(CRP)***, an acute phase protein, is a non-specific marker of chronic inflammation primarily regulated by IL-6. CRP may contribute to a pro-neoplastic environment by inducing DNA damage, promoting angiogenesis, and favoring neoplastic spread and metastis.[54] The pro-inflammatory phenotype propagated by these biomarkers is: a) more prevalent in BCS than noncancer controls,[63] b) associated with increased BC incidence, recurrence, progression and mortality[51,52,64-66] and c) associated with increased CVD risk[53] and mortality[67] via its contribution to the atherosclerotic disease process.[68] Aerobic PA is associated with amelioration of this pro-inflammatory phenotype.[55,69] Although the exact underlying mechanisms are unknown, hypothesized effects include: PA-associated reductions in visceral fat mass; increased production and release of anti-inflammatory cytokines from contracting skeletal muscle and reduced expression of Tolllike receptors (TLRs) on monocytes.[55] **Cardiometabolic biomarkers.** Higher levels of blood glucose (BG), triglycerides (TG), and total cholesterol (TC) and lower HDL-cholesterol (HDL-C) are associated with increased risk of cardiovascular events.[70-77] Regular PA improves liver, skeletal muscle and adipose tissue sensitivity to insulin resulting in decreased fasting insulin levels and the insulin response to glucose, resulting in increased glucose disposal rates.[78] PA may improve lipid profiles via a number of mechanisms including enhancing skeletal muscles' ability to utilize lipids, increased lipoprotein lipase activity and increased lecithin-cholesterol acyltrans.[79]

Impact of intervention and PA dose on biomarker outcomes. Understanding the dose of PA needed for specific outcomes in cancer survivors and whether this dose varies by participant characteristics has recently been identified as a high research priority by NCI.[80] The typical approach of testing multiple intervention components delivered simultaneously in a randomized control trial (RCT) only allows us to draw conclusions about an entire treatment package when each intervention component may differentially influence intervention adherence, PA dose engaged in and health outcomes. By testing the individual effects of PA intervention components (i.e. coaching calls, text messaging, breast cancer specific app, group support and online gym membership) on BC

progression and cardiometabolic biomarkers and examining potential mediators and moderators of these relationships in the proposed study, we will gain important insight into the "dose" of: a) PA (i.e. intervention adherence and PA volume) needed to improve biomarkers of interest and b) intervention [i.e. which components, at what levels, in what combination(s)] needed to achieve these outcomes. We will also gain preliminary insight into whether the needed PA and intervention dose varies by individual characteristics. This will allow for more specific and personalized intervention prescriptions for specific outcomes for BCS.

Dried blood spots. Remotely-delivered, technology-supported interventions have greater potentially scalability than intensive, on-site interventions and allow for larger sample sizes and greater geographic diversity. In contrast, the cost and logistics associated with collecting biomarker samples, often restricts the assessment of these outcomes in larger-scale technology-supported interventions. The self-collection of DBS—drops of whole blood collected on filter paper from a simple and inexpensive finger prick—proposed in this study provide a minimally invasive, low cost, feasible and more generalizable method[81] for measuring biomarkers in the context of a remotely-delivered PA intervention with a nationwide sample of BCS. Thus, findings will be more generalizable than other PA studies incorporating biomarkers in BCS.

Research Team. The PI, Dr. Phillips, has extensive experience designing and conducting similar physical activity studies in older adults and breast cancer survivors. The co-investigators are nationally and internationally recognized experts in cancer survivorship (Penedo, Cella), behavioral interventions (Spring, Ackermann, Penedo), mHealth (Spring), fractional factorial designs/methodology (Spring), and D&I sciences (Ackermann).

2.2 Preliminary data.

Evidence for the use of SCT. The PI's dissertation used a 6 month prospective study design to test whether the SCT model using the structural pathways proposed by Bandura[35] explained changes in PA in a nationwide sample of breast cancer survivors. Results from this study indicated SCT explained 41% and 49% of the variance in PA at baseline and follow-up, respectively.[15] Self-efficacy was the strongest predictor of PA and these effects were both direct, and indirect, via social support, goals and outcome expectations.[15] Findings were largely consistent among changes in constructs over the 6 month period and when using accelerometry to measure PA.

Feasibility of recruitment and assessment via Army of Women©. The PI's dissertation also supports the feasibility of recruiting breast cancer survivors via the Army of Women© and completion of the same, or similar, assessments to those in the present study. Within 12 hours of recruitment initiation for this study, 2,500 women expressed interested in participating and recruitment was halted due to capacity limitations. Of that number, 1,631 (64%) responded to screening and qualified to participate. I randomized 500 of those women to wear accelerometers for 7 consecutive days. Only 4 refused to wear the device. At baseline and follow-up, 1,527 women (94%) completed more than half of the on-line questionnaires. Valid accelerometer data were obtained from 442 (89%) women at baseline; 370 (83.7%) of those women also had valid data at 6 month follow-up.

Reasons for missing accelerometer data at baseline and follow-up, respectively, were: did not wear (n=36 and n=40), insufficient valid wear time (n=8 and n=17), accelerometer malfunctioned (n=5 at both), lost in mail or by participant (n=4 and n=5) and submerged in water (n=1).

Feasibility of mHealth intervention. Data from Pew[82] indicate that, as of January 2014, 58% of Americans own smartphones and 42% own tablet computers suggesting that a large proportion of breast cancers likely own this technology. Since we are recruiting from the Army of Women© which communicates via e-blasts, we expect these women to be relatively tech savvy and interested in mHealth interventions.

DBS are valid for proposed biomarkers. In studies using self-collection of DBS, ≥90% of participant samples[83,84] have been adequate for analyses indicating this is a highly feasible method for DBS collection. Dr. Funk's has rigorously tested the performance parameters of the proposed immunoassay protocol for IL-6, IL-10 and TNFα to determine the limit of detection [range: 0.3 pg/mL (IL-6) to 1.25 pg/mL (TNFα)], and assay linearity [range: 99.0% (IL6) to 113% (IL10)]. Levels of within-assay precision and between assay variation are displayed in Table 1. Performance parameters of the proposed CRP immunoassay by the Laboratory for Human Biology Research (LHBR) have also been rigorously evaluated to determine the limit of detection (0.03 mg/l), within- (95.9%) and between- (109%) assay variance and assay linearity (95.4%-109% of expected). The relationship between DBS and matched-serum CRP levels is strong and linear (R= 0.96). The University of Washington Department of Laboratory Medicine (UWLM), who will quantify cardiometabolic biomarkers, found high correlations between TG (R = 0.97) and BG (R= 0.90) in matched DBS and plasma samples. However, correlations between matched DBS and serum samples for HDL-C (R=0.55) and TC (R=0.58) were less optimal[85] which was unexpected, given higher correlations were observed in comparisons using samples analyzed under controlled laboratory conditions. The reason for this discrepancy is unclear, but new assay standards are developed and these relationships are being re-established.

Table 1. Assay Precision of DBS

Assay	High CV	Med CV	Low CV
Within-assay precision			
IL-6	8.98	9.73	9.34
IL-10	10.91	12.92	14.85
TNF-α	6.78	8.47	21.49
Between-assay variation			
IL-6	4.34	8.51	3.41
IL-10	5.41	13.85	7.89
TNF-α	7.56	3.65	2.62

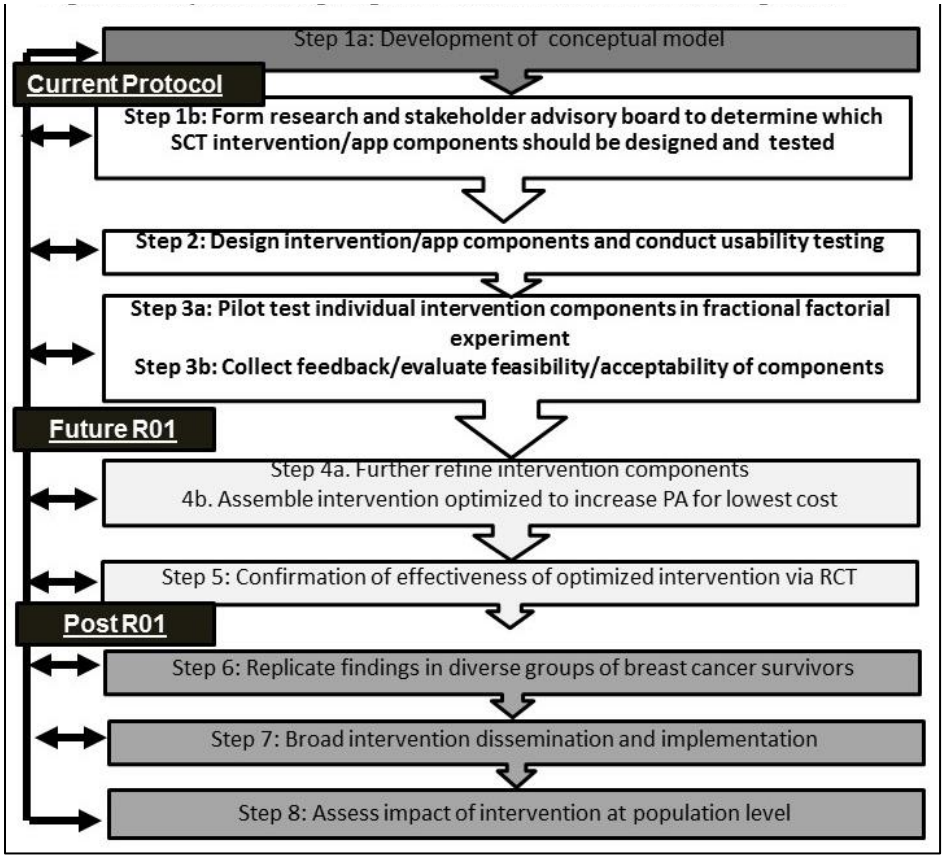
Summary. Our preliminary work provides evidence for the use of SCT to guide intervention design and demonstrates the feasibility of enrolling/retaining and assessing participants using Army of Women©. National smartphone usage data suggest the acceptability of a mHealth PA intervention.

2.3 Significance and Innovation

The proposed study is significant because it represents the first systematic effort to use optimization methodology to design a theoretically-guided mHealth PA intervention for breast cancer survivors with D&I in mind from the outset. Ultimately, this work will significantly contribute to our understanding of how to effectively increase and maintain PA to improve health and disease outcomes in breast cancer survivors.

Methodological Innovation: MOST to Design with D&I in mind from the Start. Intervention development typically consists of designing an intervention with multiple components and then testing whether the intervention, as a whole, has a significant effect in randomized clinical trials (RCT).[86] However, information about which intervention components contribute to the desired effect and which do not is necessary to continue to increase intervention effectiveness and efficiency. Because all intervention components are turned "On" in the treatment group and "Off" in the control group in a typical RCT, this information cannot be obtained. The Multiphase Optimization Strategy (MOST)[25,87] is a comprehensive framework that supports optimizing an intervention by efficiently and systematically identifying the most promising intervention components and component levels. MOST is based on is based on the engineering principles of resource management and continuous optimization. The overall goal of MOST is to maximize public health impact (efficacy x intervention reach) using available resources. MOST is an emerging methodology that may be particularly useful for designing mHealth interventions with D&I in mind from the start because of its emphasis on optimization, an iterative design process and public health impact.[20,88] Figure 3 describes how we plan to use MOST to design an optimized PA intervention for breast cancer survivors. MOST, like all theory-based approaches to intervention development, starts by using theory, scientific literature, clinical experience, and results from previous studies to establish a conceptual model (Step 1a). Based on prior work, we am proposing to use SCT for this study. We will complete steps 1b to 3b as part of the proposed project. Step 1b will involve further refinement of the model/component selection to inform Step 2, intervention/app design and usability testing. These steps will be performed in collaboration with relevant stakeholders (cancer survivors, clinicians, research experts). Step 3a will pilot test the feasibility, acceptability, and effects on PA and important patient reported outcomes (PROs) of each of the intervention components and component combinations. Step 3b involves collection of participant feedback and evaluation of the intervention components and combinations. The present study will provide the necessary preliminary data to apply for future grants steps 4a-5. The MOST framework has rarely been applied to the development of behavioral interventions, and to the best of our knowledge, has never been specifically applied to the development of a PA intervention in cancer survivors.

Figure 3. Steps for Designing with Dissemination in Mind Using MOST



Conceptual and Technological Innovation. Existing evidence indicates that: (a) home-based interventions can effectively increase PA among breast cancer survivors[5] and (b) mHealth supported interventions are effective for increasing PA.[89-91] However, to the best of our knowledge, there have been no tests of mHealth supported PA interventions in breast cancer survivors. As cellphones are becoming ubiquitous,[82] they may offer a cost-effective tool to change and maintain PA behavior in a manner that increases intervention reach and D&I potential.[88,92] Moreover, mHealth interventions allow researchers to collect real-time data and provide real-time feedback. Those capabilities can: a) provide additional insight into relationships between PA and PROs, b) increase safety by alerting researchers immediately to problems, c) allow better monitoring of intervention adherence and d) increase adherence. While many commercially available PA apps exist, the majority have not been empirically tested, are not evidence-based, theoretically-guided or designed specifically for cancer survivors.[93-95] Therefore, the feasibility, acceptability and effectiveness of mHealth PA interventions needs to be tested in cancer survivors. Selection of mHealth intervention components will be guided by SCT, engage stakeholders in development, and incorporate cutting edge technology and functionality to determine, not only whether a mHealth intervention is associated with PA change and maintenance, but which components maximize these outcomes for the lowest cost.

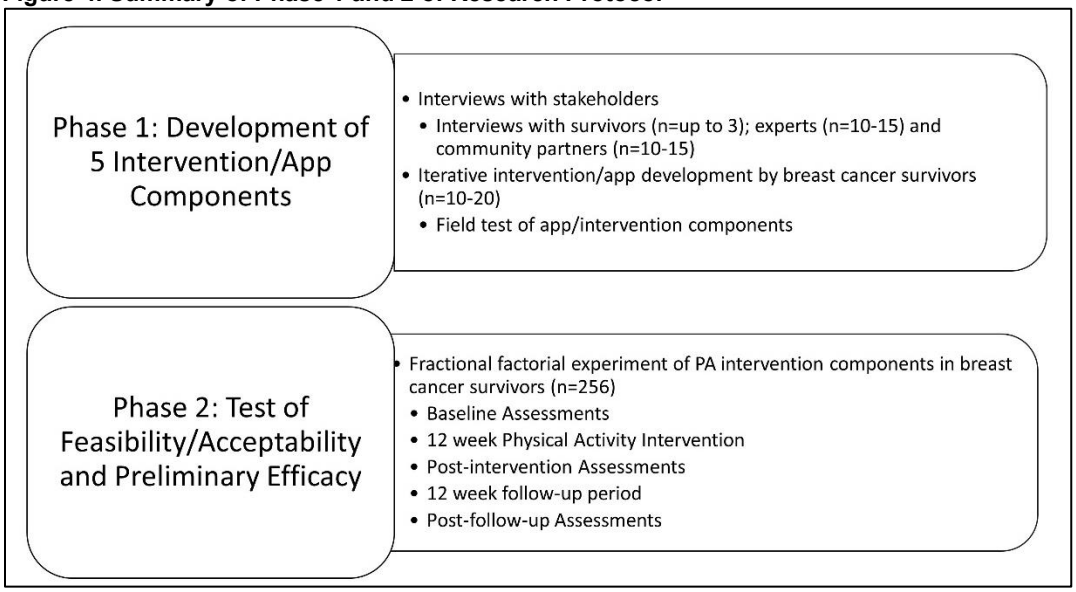
3.0 Inclusion and Exclusion Criteria

3.1 Screening for Eligibility

This study will have two phases (see Figure 4). Phase 1 (Aim #1) will involve intervention development. Phase 2 (Aims #2, #3 and Exploratory) will involve the pilot testing of the intervention components to be identified in Aim #1.

Phase 1 and Phase 2. For both phases, interested participants will be screened for eligibility either via an on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

Figure 4. Summary of Phase 1 and 2 of Research Protocol



3.2 Inclusionary and Exclusionary Criteria

This study will have two phases (see Figure 3). Phase 1 (Aim #1) will involve intervention development. Phase 2 (Aims #2, #3 and Exploratory) will involve the pilot testing of the intervention components to be identified in Aim #1.

Breast Cancer Survivors in Phase 1 and 2. The same inclusionary criteria for breast cancer survivors will be used for all phases of the research. However, all women recruited into the intervention in Phase 2 will also be required to pass the *Physical Activity Readiness Questionnaire (PAR-Q)*[96] (see attached) or receive medical clearance from their primary care physician or oncologist.

Inclusionary Criteria for Breast Cancer Survivors:

- Women ≥ 18 years of age who were diagnosed with Stage I-III breast cancer within the last 5 years
- Have completed last cancer treatment (adjuvant chemotherapy, radiation therapy or surgery) at least 3 months prior to enrollment
- English speaking
- Currently participate in <60 minutes of moderate and vigorous PA/week (Phase 2 only)

- Own a smartphone (For Phase 2 only: iPhone –version 5 or greater or an Android –version 5 or greater)
- Have access to a computer with Internet
- Participants may be using adjuvant endocrine therapies.
- Willing to be waitlisted for future wave if current wave reaches capacity (Phase 2 only)

Exclusionary Criteria for Breast Cancer Survivors:

- Women will be excluded if they report any of the following:
    - Respiratory, joint or cardiovascular problems precluding PA
    - Metastatic disease
    - Planned elective surgery during duration of the intervention/follow-up that would interfere with participation (e.g., breast reconstructive surgery).
    - ONLY IF PARTICIPATING IN OPTIONAL DBS COLLECTION:
        - A prior cardiovascular event (i.e. stroke, myocardial infarction)
        - Have been diagnosed with an acute or chronic immune system medical conditions, or conditions that impact immune and endocrine function (e.g., CFS, Lupus, rheumatoid arthritis, Hepatitis C, or immunosuppressive treatment requiring conditions)

Inclusionary Criteria for Other Stakeholders in Phase 1:

- English-speaking
- Have expertise in breast cancer or physical activity OR organization the individual works for actively works with breast cancer survivors on a regular basis
- Own a smartphone

Inclusionary Criteria for "Buddies":

- Must be at least 18 years old
- Have access to a computer and internet
- Own a smartphone
- Be willing to receive regular emails from the study team
- Be willing to wear a Fitbit and transmit Fitbit data to the study team
- Be willing to "friend" participant in the Fitbit app and provide support and encouragement to the participant.

3.3 High-risk Subpopulation Inclusion.

The following subgroups will be excluded from the present study:

- Adults unable to consent
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners

4.0 Study-Wide Number of Subjects:

Phase 1. We will recruit stakeholders including breast cancer survivors (n=30 for interviews; up to 100 for usability testing), experts and clinicians (n=10-15; e.g.

oncologists, nurses, experts in D&I, PA and rehabilitation) and representatives (n=10-15) from local community organizations (e.g. Gilda's Club Chicago, the YMCA and American Cancer Society Illinois Chapter).

Phase 2. We plan to accrue a nationwide sample of 256 women to the intervention pilot testing phase. Approximately 50% of these will be assigned to the buddy condition. As such we will accrue 128 buddies. We anticipate 80% of these "buddies" (n=102) will agree to participate in the optional questionnaire assessments. We will recruit up to 35 participants for the post-intervention interviews.

5.0 Study-Wide Recruitment Methods:

5.1 When, where and how potential subjects will be recruited.

Phase 1. Women will be recruited from the Army of Women (AOW) e-blast.© The AOW is an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women. Of these, ~30% (112,500) self-report a breast cancer history. Women interested in participating in the current study will respond to the e-blast consenting to have their contact information released by the AOW to study investigators. Their contact information will, then, be forwarded to the study investigator who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

Community representatives will be recruited in conjunction with NU's Center for Community Health (led by Co-I Dr. Ackermann) via personalized e-mails and phone calls. Experts will be recruited through the RHLCCC and the PI's, co-investigators' professional networks via listservs and personalized e-mails and phone calls.

Phase 2. Breast cancer survivors will be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study investigator who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

If our recruitment goals are not being sufficiently met via the Army of Women© we will also post study fliers and advertisements on social media sites (i.e. Facebook, PatientsLikeMe) and on-line forums (i.e. Sisters Network, Nueva Vida, Living Beyond Breast Cancer). In addition we will send recruitment emails to all women from previous studies who consented to being contacted regarding future study opportunities. All women who are recruited through these alternative strategies will be instructed to contact

the study staff who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

- **Buddy recruitment:** Breast cancer survivors assigned to the Buddy component, will be asked to contact their buddy and provide the study team with the name and email address of their chosen buddy. The buddy will then be emailed a brief description of the study and a link to the on-line buddy screening RedCap. Interested and eligible buddies will be offered the opportunity to participate and will complete informed consent. If a buddy indicates, they are not interested or fails to respond after 3 contact attempts, we will ask the participant for a new buddy name and email address.
- **Post-intervention interview:** Individuals who participated in the Fit2Thrive intervention within the previous 6 months and agreed to hear about future studies will be eligible. Women will be invited to participate via email. They will be selected for invitation based on adherence to the program and intervention component assignment to ensure broad representation. Former participants will be contacted up to 3 times to participate after which we will cease contact.

5.2 Methods used to identify potential subjects.

Women who meet the following criteria will be included in the present study: a) indicate they are interested in the present study, b) meet all eligibility criteria and c) consent to participation.

“Buddies” who meet the following the following criteria will be included in the present study:) indicate they are interested in the present study, b) meet all eligibility criteria and c) consent to participation.

5.3 Recruitment materials.

All recruitment materials will list study eligibility criteria and requirements, will provide a link to the study web-page and will not deviate from the IRB-approved language. The posting will also include a phone number and study e-mail address where participants can reach staff if they have any general questions regarding study participation.

6.0 Multi-Site Research: N/A

7.0 Study Timelines

7.1 Duration of an individual subject’s participation

Phase 1. We will select 30 women to participate in interviews from those interested. We anticipate survivor interviews will last 45-60 minutes. We anticipate expert/clinical stakeholders and community/advocacy partner interviews will last approximately 30-45 minutes. Survivors who participate in the app development process (n=100) will participate in up to two app development sessions (approximately 1 hour each) and

possibly a field testing of the app/intervention components (duration of 5 to 14 days). During the field testing, participants, will spend approximately 30-60 minutes interacting with the study app each day including entering information and providing real time feedback to developers on features they do and do not like. There is a chance saturation/consensus will be reached during the field testing before all survivors have had a chance to participate. Therefore, some survivors may not participate in the field testing and post-field testing app development session.

Phase 2. Survivors will participate in a 12 week intervention and a 12 week follow-up for a total of 24 weeks. Buddies will provide support to their participant throughout the entire 24 week period. Women who participate in the post-intervention interview, will participate for approximately 30-45 minutes.

7.2 Duration anticipated to enroll all study subjects.

Table 2 details the full study timeline. Specific details for each phase are as follows:

Phase 1. We anticipate it will take 3 months to recruit/complete initial interviews, 3-6 months to design/refine and program intervention/app components, and 3 months to conduct several field trials with breast cancer survivors (n=100). We have planned 12-18 months for intervention/app development and will meet bi-weekly with developers to ensure sufficient progress towards this goal.

Phase 2. We anticipate it will take 18 to 24 months to recruit and enroll breast cancer survivors and buddies into the intervention pilot phase of the trial. We anticipate it will take approximately 6 months to enroll all women in the post-intervention interviews.

Table 2. Study Timeline

		Year 1				Year 2				Year 3				Year 4				Year 5			
Quarter		**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
App Development (Phase 1)	Study Preparation																				
	App/Component Development/Refinement																				
Intervention Component Piloting (Phase 2)	Recruitment/Baseline Data Collection																				
	Active Intervention Component Delivery																				
	Follow-up Period																				
	Data Analyses																				

7.3 *Estimated date for study completion:* **June 30, 2020**

8.0 Study Endpoints

8.1 Describe the primary and secondary study endpoints.

Primary study endpoint: intervention feasibility/acceptability.

Feasibility: This will be measured during the intervention, immediately post-intervention and after the follow-up period. Measures include:

- *Intervention reach*: # of participants enrolled/# of eligible individuals
- *Participant retention*: # of participants who drop out/# of participants randomized

- *Intervention Adherence*: % of weeks adhered to exercise prescription during intervention period
- *Intervention Maintenance*: % of weeks adhered to exercise prescription during follow-up period
- *Intervention component engagement:*
    - During intervention: # of times, on average, participants interacted with each intervention component during intervention
    - During follow-up: # of times, on average, participants interacted with each intervention component during follow-up
    - Total: # of times, on average, participants interacted with each intervention component over intervention and follow-up

Acceptability: This will be measured via a process evaluation immediately post-intervention at 12 weeks and after the follow-up period at 24 weeks. This evaluation will assess the following:

- Perceived effectiveness of intervention components/app; use of app/intervention materials; plans to continue PA/app use; elements of intervention liked/disliked; satisfaction with program delivery, assessments and staff

Secondary study endpoints: Secondary study endpoints include physical activity (self-report and objectively measured), social cognitive theory constructs (self-efficacy, outcome expectations, social support, physical activity enjoyment), patient-reported outcomes (fatigue, health-related quality of life, cognitive functioning, physical functioning and depression) and BC progression and CVD risk biomarkers. Secondary study endpoints will be assessed at baseline, post-intervention and at the end of the follow-up period. We will also assess covariates including demographic (i.e. marital status, number of children, height, body weight, occupation, age, income and education), breast cancer characteristics and history (date of diagnosis, type of treatment, length of treatment, disease stage, tumor receptor status, recurrence, etc.) and general health history (i.e. comorbid conditions, height, weight, fruit and vegetable consumption, smoking history, etc.) Covariates will be assessed at baseline.

8.2 Describe any primary or secondary safety endpoints: N/A

9.0 Procedures Involved*

9.1 Study Design.

Table 3. SCT Construct and Potential Intervention Component to Target	
SCT Construct	**Potential Intervention Component to Be Turned "On/Off"**
Self-efficacy (1 component)	-Daily feedback on PA accomplishments -Weekly motivational stories about similar survivors -Support for interpreting physiological responses (i.e. heart rate, muscle soreness) to PA -Messages with weekly PA tasks to master
Outcome Expectations (1 component)	-Text messages providing information on expected progress -Weekly collection/feedback on outcome of interest (e.g. mood)
Goal-setting (1 component)	-Daily PA tracking using a FitBit -Weekly goal-setting prompts/feedback on progress -Prompts to schedule PA for the day

Facilitators/ Barriers (2 component)	-Choose exercise "buddy" to participate in intervention with -Daily tracking of facilitators/barriers -Group or individual competitions or games -Message boards for between-participant communication -Problem solving support calls -"On demand" motivational messages -Virtual, on-line gym membership

Phase 1. This portion of the study will consist of interviews and app/ intervention/ development. Initial interviews with breast cancer survivors, experts and community partners will be conducted before app development begins. The purpose of these sessions will be to obtain stakeholders' perceptions of the intervention/ app components proposed in Table 3, identify new potential components and decide on 5 components to test. Survivors will also be selected to participate in a stakeholder advisory board session to inform decisions related to Phase 2 of the study. We have attached guides for the initial interviews. At the end of the interviews subject will also be asked if they are interested in participating in the advisory board (survivors). **Phase 2.** Following Phase 1, we will conduct a pilot experimental test of all components to evaluate their feasibility and accessibility (Aim 2) and preliminary effect on PA (Aim 3) and PROs (Exploratory Aim) at 12 weeks and 24 week follow-up in a sample of 256 breast cancer survivors using a MOST design (See Table 6).

9.2 Research Procedures

Phase 1

We will engage survivors in developing and tailoring system components to fit their needs employing three user-centered design principles: 1) Focus on Users and Tasks, 2) Measure Usability Empirically and Design and 3) Test Usability Iteratively.[97] Similar procedures have been followed as part of app development for Dr. Spring's existing, effective mHealth interventions. Additionally, since similar components have been developed/used in interventions conducted by Dr. Spring's research team, the development process will consist largely of tailoring/refining these components for the present study.

Table 4. Usability Measures

Factor	Objective Measures	Subjective Measures
		Users' rating of…
Learnability: ease with which use of device is earned so users can rapidly accomplish intended tasks	Time taken for users to learn to accomplish intended tasks	Ease and time to learn system
Effectiveness: usefulness for supporting intended tasks	Successful performance of intended task (y/n)	System's ability to promote performance and productivity
Efficiency: productivity once users have learned the system	Time to accomplish tasks once have learned system	System's ability to improve speed at which they perform
Errors: low frequency, severity of errors and easy recovery	Error rates trying to use system; severity of errors; recovery time for errors	Impact of errors on using system and ability to recover from errors
Flexibility: variety of ways to achieve intended tasks	Number of different command or routed to achieve same goal	System's ability to provide different command or routes to achieve same goal
Memorability: ease with which casual users can return to the system without having to relearn	Memory failure rate on how to use system next time; time to re-learn system after periods of non-use	Ability to remember how to use system next time and ability to re-learn system after periods of non-use
User Satisfaction: pleasant for users	Frequency for utilization of the system and its features	Fondness, perceptions and opinion of system and its features

Assessments

Interviews: We are currently conducting an online needs assessment that will inform this study. To further inform our design, we will conduct interviews with stakeholders (survivors, experts, community partners) to inform the development of intervention components that are grounded in SCT. Expert/community partners' interviews will take place in-person on Northwestern's Chicago campus whenever possible. However, we anticipate that the clinical/research

partners' and community/advocacy partners' interviews may be hard to arrange so these sessions may occur via the telephone or web (i.e. Skype), at the partner's workplace or at some other public location (i.e. library, coffee house). Breast cancer survivors' interviews will be completed via telephone. Because we anticipate interest will be greater than capacity, we will select 30 women of the up to 100 women recruited for interviews. All stakeholders will complete informed consent on-line. Interviews will provide input and feedback on desired intervention components as well as components identified in Table 3. Stakeholders will provide insight into implementation of physical activity programs within their setting and feedback the perceived usefulness of these components, identify potential alternative components, and aid in tailoring intervention content to their needs. survivors to participate in a stakeholder advisory board session to further vet intervention components.. Community and expert stakeholders will also be provided with a study information sheet at the end of their interview for their reference. The interview will take 45-60 minutes for community partners/experts and 30-45 minutes for survivors.

App Development Session 1: Following completion of the interviews with the survivor subgroup, all survivors will be invited to participate in the first app development session which will be a two-part on-line survey. The first part will ask survivors to provide feedback on their preferences and opinions for app features. The second part will present wireframes of potential components and solicit input on their perceived usefulness and effectiveness. All women (n=100) will participate in this session. Both parts of the session will take up to 60 minutes to complete. We will use these data to work with programmers and breast cancer survivors in an iterative manner to create a minimally viable test version of the intervention components. All components selected for testing will meet the following criteria: a) hypothesized to target one primary SCT construct and enhance PA adherence via pathways detailed in Figure 1; b) have a clear relative advantage in terms of influence on PA and cost/burden and c) are approved by stakeholders. Participants will be sent an initial e-mail with a link to the survey and up to 3 additional reminder e-mails to complete the survey.

Breast Cancer Survivor Stakeholder Advisory Board Session : Survivors will be sent an email asking them to participate in a conference call to go over an executive summary of findings from the interviews and App Development Session 1. This session will ask survivors their opinions on the proposed app and intervention components (see attached guide). The conference call will be audio recorded and then be used to reach consensus before proceeding with initial development of the app prototype.

Field Test: Survivors (n=100) will participate in an app field test. They will be assigned in waves of up to 20 women to use the intervention components for up to 2 weeks. During the field test, survivors will provide feedback to developers in real time when they are using the app regarding features they do and do not like and app functionality. At the end of each wave, the research team and developers will ask participants to complete an on-line survey and participate in a telephone or web-based session to solicit feedback on the usability components identified in Table 4. Based on these data, the intervention components will be tweaked. The new iteration of the intervention components will be tested by the next wave using the same procedures until all participants have tested it, or

we have reached saturation (n=up to 100). Thus, all survivors may not participate in this session. The purposes of this field study is NOT to test how well it works to increase PA, but rather to evaluate the app's functioning and ease of use in everyday life. Participants will be explicitly instructed NOT to change their usual physical activity patterns as part of this field test. They may be asked to enter some data on your behaviors, motivation and symptoms to test functionality of these components. However, participants will be explicitly instruct that these data do not necessarily need to reflect their true ratings. These data will not be used for any purposes other than to test the functioning of the app. Participants will spend approximately 15-60 minutes interacting with the app each day during the field test which will include providing any feedback to developers in real-time, as they use the app, regarding features you do and do not like and functionality. Prior to the initiation of field testing participants will be sent an update e-mail and asked to indicate whether they own a Fitbit and how tech savvy they are so this information can be taken into account when reviewing their responses.

App Development Session 2: Immediately after completing the field test, survivors will be asked to complete an on-line survey and/or attend a telephone or web-based session to provide feedback on the intervention features they liked and disliked and any ideas they have on what could be changed and/or improved. Depending on the ability to schedule survivors this may be individual or involve up to 20 other survivors. This session will last up to 60 minutes.

- *Wave 1* (n=10) *and Wave 3* (n=10-20) *of Field Testing and App Development Session 2:*
    - *For the field test:* Participants will be sent an email notifying them they have been selected and asking them to download and use the test version of the app for a minimum of 3 days over the course of a 7-10 days. Participants will be provided with instructions on how to download the app and provide feedback to the study team in real-time.
    - *For App Development Session 2:* At the end of that period, participants will be sent the app post-field test survey and asked to complete it.
    - Participants will be sent up to 3 reminders for each of the following tasks: using and providing feedback on the app and completion of the field test survey.
- *Wave 2 of Field Testing* (n=10-15) *and App Development Session 2:*
    - *For the field test:* Participants will be sent an email notifying them they have been selected and asking them to complete the App Notification Field Test Survey. Participants will be sent up to 3 reminders to complete the survey.
    - *For App Development Session 2:* Wave 2 participants will not complete this since they are not using the app.

Women will be contacted to schedule participation in each session via phone or e-mail.

Because the design process is iterative and the content of each session is dependent on prior sessions, materials for each session will be submitted to the IRB as they are developed.

Retention Strategies. In order to enhance subject retention we will occasionally send greeting cards for various holidays (i.e. Winter holidays, Thanksgiving, Breast Cancer Awareness month, birthdays, etc.) or milestones (i.e. study completion, half way through the study, etc.) via the USPS or an on-line service (i.e. Paperless Post or Evite). All greeting card language will be submitted and approved by the IRB prior to sending to participants.

Monitoring subjects for safety for Phase 1
This study is classified as minimal risk because the probability and magnitude of harm or discomfort anticipated is not greater than those ordinarily encountered in daily life. For participants who engage in interviews, it will be made clear that all of their comments will be kept confidential and de-identified. They will also be instructed that they do not have to answer any questions that make them uncomfortable and that they can withdraw from the study at any points. For breast cancer survivors who will engage in intervention/app development and will be directly observed performing tasks and answer questionnaires, the same procedures as detailed, below for Phase 2 will be followed.

Phase 2

An overview of the flow of participants through the study is provided in Figure 5.

Screening
Women who express an interest in participating in the Fit2Thrive intervention via the Army of Women© will be sent an email with a brief study description and eligibility criteria. This email will also contain a link to the on-line (RedCap) Screening. The first part of the screening will provide an in-depth overview of the study. After viewing these materials, potential participants will first confirm interest in research participation and proceed to complete screening questions assessing for eligibility criteria (e.g., demographics, cancer diagnosis, age). After an individual passes the initial screening, they will automatically be redirected to complete the Physical Activity Readiness Questionnaire (PAR-Q).[96] Once completed, they will provide detailed contact information and scheduling availability. Scored PAR-Q responses will be reviewed to determine if physician approval is required prior to participation. Those who require approval will be flagged for follow-up.

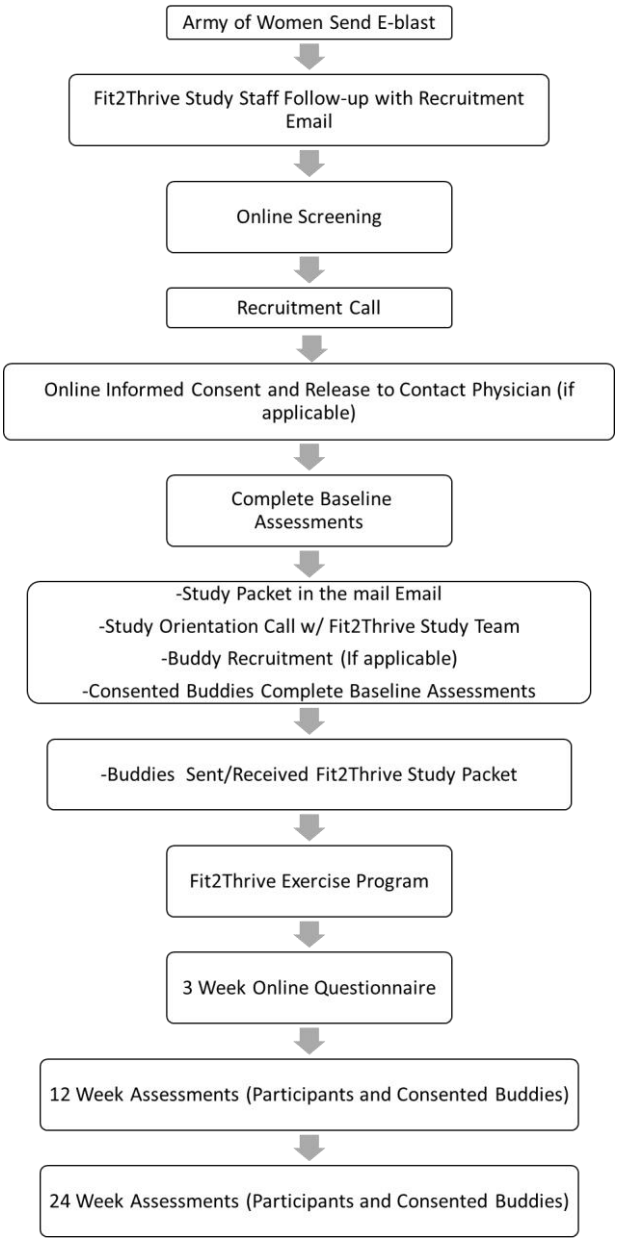
- ***If not ineligible*:** Participants will be thanked for their interest and directed to on-line resources for physical activity and nutrition for cancer survivors.
- ***If eligible*:** Participants will be receive a study orientation call. Prior to this call, they will be sent a copy of the informed consent and a study overview handout.
- ***Attempts to contact***: Study staff will make up to three email attempts to reach potential participants to complete the web screening. If unable to reach after the third attempt, study staff will mark the individual as "ineligible," with the reason as "unable to contact."

Recruitment Phone Call
Because participants will be recruited from all over the country, the orientation session will occur remotely via a telephone call. Prior to the call, study staff will email participants a copy of the informed consent and a study overview. During the call, study staff will

introduce what is required for study participation and provide instructions for completing baseline assessments. If they failed PAR-Q screening, they will also be instructed that they will need to obtain physician consent prior to participation. This session will take approximately 10-15 minutes.

- ***If still interested*:** Participants will be sent a link to the on-line consent form. If they failed PAR-Q screening, they will also be sent a link to a RedCap form to consent to allowing study staff to contact their physician and provide physician contact information.
- ***If no longer interested:*** They will be thanked and asked if they would be willing to be contacted regarding future study opportunities.
- ***Attempts to contact***:
    - Study staff will make up to three call attempts to reach potential participants for the orientation call. If they are not reached at this point, staff will follow-up with one last call and email.
    - Study staff will make up to three e-mail attempts to reach potential participants to complete the informed consent. If unable to reach after the third attempt, study staff will call the participant and send one final email. Those who we are unable to reach after these attempts will be marked as "ineligible," with the reason as "unable to contact."

Figure 5. Participant Flow Through Study



Assessments

After completion of informed consent, women will be e-mailed baseline study questionnaires via RedCap and notification that their accelerometer packet has been placed in the mail. The accelerometer packet includes: accelerometer, accelerometer instructions, accelerometer log, printed copy of the informed consent, a self-addressed stamped return envelope to return the accelerometer. Questionnaires will take approximately 30-45 minutes to complete and participants will be asked to complete the on-line study questionnaires within 10 days of receipt. They will be asked to wear the accelerometer for 7 consecutive days starting on the day indicated on the log and mail it back to study investigators at the end of the 7 days period.

Women will also have the option to participate in the self-collection of a 2.5 mL blood sample to be collected by pricking their finger with a retractable lancet and placing 5, 50 µL spots of blood on a sample collection card. They will be mailed all materials needed to collect the blood spot (i.e. lancet, alcohol swab, band-aid) and written instructions with pictures for collecting and returning the sample as well as a self-addressed stamped envelope.

The same procedures will be followed for 12 week post- intervention and 24 week follow-up data collection.

- ***Attempts to contact***: Reminder calls or emails will be conducted if questionnaires and/or accelerometers are not received within the specified time period until the activity monitor is returned. Reminders for questionnaires will cease after the activity monitor is returned unless the participant has received less than 3 email reminders and one phone/email reminder. In these cases, the participant will be contacted via email 3 times and also receive one final attempt via phone and email.

Randomization
Participants will be randomized after they have completed all baseline assessments using a computer-generated minimization allocation method to ensure balance in treatment groups.

Participants will not be informed they are being randomized. Instead, they will simply be told about the core intervention and the potential to have other intervention strategies. We have decided not to disclose randomization for the following reasons: a) being randomized does not influence study risk, b) all participants receive the core intervention at a minimum and c) we hope to minimize attrition. Additionally, this will help to streamline the study description and, hopefully, prevent any confusion regarding the study design.

Study Packet Mailing
Participants will be sent an email informing them their study packet has been placed in the mail and a study team member will be calling them shortly. If they are assigned to the buddy condition, this email will include a link to complete the Buddy Selection Survey, and they will be provided with a recruitment email to forward to their buddy.

The study packet will containing the Fitbit and paper instructions for downloading the study app, setting up the Fitbit and for using all components to which they are assigned.

Ideally, they will receive the packet prior to the study overview call, but this will not always be the case. If timing does not allow for this, we will email the instructions to participants prior to the overview call.

Study Orientation Phone Call

Study staff will call all study participants to go over in greater detail the strategies to which they have been assigned. This call should take approximately 10-15 minutes.

Intervention Launch Reminder/Tech Check-In
Participants will be sent an email reminder that the intervention is launching 7-10 days prior to the study start date and will be reminded to contact study staff if they are having any technical difficulties. They will also be called or emailed reminders if they have not downloaded the app prior to the intervention start date or used the app on Day 1 or Day 2 of the intervention.

Intervention Components
CORE intervention. The CORE will be delivered to all participants to build essential competencies needed to increase physical activity safely. The CORE will include the following:

- *Educational website*: This will provide participants with information and knowledge about the benefits for physical activity, safely progressing through an exercise program and strategies for effectively changing and maintaining physical activity behavior (i.e. social support, goal-setting). This site will be available as a standalone site and embedded within the app.
- *Basic smartphone app*: Features of this app include, but are not limited to, the ability to monitor and track physical activity, pre-specified weekly physical activity goals and feedback on progress.
- *Fitbit:* Participants will be instructed to wear the device on the provided belt clip or wristband during all waking hours every day of the study to assist in monitoring and tracking physical activity. The Fitbit will communicate with the app so data are integrated.

Participants will also be randomized to receive the following components:

1. App+: Participants assigned to this component will receive a "deluxe" version of the app. This will include all of the features of the basic app plus additional app modules listed below.
    a. *Weekly Goal-Setting Tool*: Allows to schedule activities for specific days of the week and set reminders for these activities.
    b. *Challenges:* Provides weekly challenges (i.e. 5,000 steps/day challenge; 5 min MVPA/day) participants can enroll in and automatically tracks progress. Progressively harder challenges become "unlocked" as participants complete less intense challenges.
    c. *Newsfeed:* Space where study staff will post content including, but not limited to, Fit Studies (lay summaries of physical activity research), Fit Survivor Spotlights (stories about women who have successfully changed their behavior), Workout Ideas and other motivational content.

2. Telephone Support Calls. Participants assigned to this component will receive a call from study staff to check-on on their progress, provide motivation and troubleshoot any issues they may have. These calls will occur bi-weekly (6 total) during the initial 12 week intervention period. All calls will be recorded for quality control.

3. "On-line" Exercise Classes: Participants assigned to this condition will receive access to a digital download for a commercially available walking DVD and suggestions for weekly workouts from the same instructor's YouTube channel on a private study YouTube playlist that will only be accessible to individuals assigned to this component of the intervention. These videos will be vetted by the research team for safety and appropriateness prior to posting. Participants will also receive a weekly survey to indicate how frequently they used this component.

4. Fitbit "Buddy": Participants assigned to this condition will select a "buddy" from their personal life (friend, co-worker, child, spouse, sibling, etc.) to help support them. The buddy will be mailed a Fitbit. Both the participant and "buddy" will receive training materials on how to make the most out of their relationship which will include how to use the social features of the Fitbit app, how to seek support (participant) and provide support (buddy), and receive bi-weekly emails (6 total) during the initial 12 week intervention period geared towards facilitating social support. Participants will also receive a weekly survey to indicate how frequently they used this component.
    a. All buddies will receive an email from the participant explaining the study, complete pre-screening and undergo an on-line consent.
        i. Buddies will be required to complete the PAR-Q and will be required to get physician consent if they fail.
    b. *Buddy Involvement:* As a "buddy" individuals will be asked to agree to the following:
        i. Complete on-line informed consent
        ii. Regularly wear the Fitbit
        iii. "Friend" the study participant on the Fitbit app
        iv. Share their Fitbit data with study investigators
            1. Fitbit study accounts for each individual buddy will be created by study staff to streamline the process of obtaining the buddy's Fitbit data. Each buddy will be asked to use the Fitbit account and password provided during their duration of participation in the Fit2Thrive Study.
            2. To fully protect confidentially, we will provide a study email address that will not include any personally identifying information to be used with the Fitbit app (i.e. F2Tbx100 and F2Tbx100@gmail.com).
            3. The RedCap study database is the only place where the identification number, the participant's name, Fitbit email and Fitbit username will appear together and will only be accessible by the investigators and used for study tracking purposes
            4. Since participants will be allowed to keep the Fitbit device at the conclusion of data collection, all participants will also be instructed on how to change their Fitbit email and username at the conclusion of the study.
        v. Provide support to the study participant

vi. Complete optional on-line surveys at baseline, 12 weeks and 24 week follow-up.

5. Text messages: Participants in this component will receive regular messages that are motivational and target SCT constructs (i.e. “The best way to stay on top of your game is by scheduling your plans! Do that here and make things easier!” ; “Exercise not only contributes to a healthier lifestyle, but it has also been shown to boost productivity and creativity. Be strong, think smart!”) and provide feedback on intervention progress (i.e.” You only met y% of your goal last week. It can be hard to fit exercise into your schedule, but remember every minute counts!”).

Follow-up

At the end of 12 weeks, participants will be encouraged to maintain PA and will have access to all “automated” intervention materials for the condition assigned. However, all regular contact from the study staff will discontinue.

Retention Plan

To prevent attrition, study staff will develop good rapport with participants during recruitment and maintain the relationship throughout the study. Participants will be provided with a phone number to call immediately if they encounter any tech issues with the application or Fitbit. Staff will convey reminders of scheduled assessments by phone or email. Participants will also be incentivized $20 to complete baseline, 12 week and 24 week assessments for a total of $60, and will be allowed to keep the Fitbit if they complete the 12 week intervention. Individuals who participate in the optional blood sample collection will be paid $15.00 at each time point ($45.00 total) upon receipt of their blood sample.

Additionally, in order to enhance subject retention we will occasionally send greeting cards for various holidays (i.e. Winter holidays, Thanksgiving, Breast Cancer Awareness month, birthdays, etc.) or milestones (i.e. study completion, half way through the study, etc.) via the USPS or an on-line service (i.e. Paperless Post or Evite).

If a participant does not track any activity via the app or Fitbit for 7 consecutive days, study staff will reach out to the participant via phone and/or e-mail. If we are unable to reach a participant after 3 phone calls or emails and a final email attempt, or they do not start recording data again after 2 weeks, we will contact the participant’s emergency/locator contacts. Participants will identify two emergency/locator contacts that may be notified if contact with the study participant is lost. Emergency/locator contacts will be associates of the participant who have a different telephone and email address from the participant and who agree to serve as emergency contacts for the participant. One locator/emergency contact must not live in the same house as the participant. We will only attempt to contact an emergency/locator contact if we are unable to reach an active participant after 3 phone call or e-mail attempts and a final email attempt, or in the event of an emergency. After these initial attempts, we will attempt to contact the participant’s designated emergency/locator contact. We will only make one phone call attempt to reach an emergency/locator contact. If we are unable to reach the contact, we will attempt to leave a voice mail.

Post-Intervention Interviews

Approximately 35 women will be selected to complete a post-intervention email. All women who have agreed to be contacted regarding future studies and have completed the program within 6 months will be eligible. Participants will be invited based on adherence level and components assignment to ensure equal distribution across these variables. Women will be invited via email. Interested women will complete on-line informed consent. Once they have consented, a study team member will follow-up to schedule an interview. Interviews will be conducted via phone or web, depending on preference and will take approximately 30-45 minutes to complete.

Monitoring subjects for safety for Phase 2

This study is classified as minimal risk because the probability and magnitude of harm or discomfort anticipated is not greater than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests and confidentiality is adequately protected. The PI and study investigators will conduct continuous review of data and patient safety. Any staff member or investigator can spontaneously identify an adverse event. Participants will be instructed to call or e-mail the PI in the event of any emergencies or medical events within 24 hours of the event occurring. These instructions will be included in all cover letters that accompany study materials and displayed prominently within the app.

Events may also be spontaneously reported to staff during contact time. Adverse events and serious adverse events may also be identified during regularly scheduled calls or emails by researchers blinded to the treatment condition of the participant. These phone interviews or emails will be conducted every 8 weeks throughout the 24 week study period. Breast cancer survivors participants will be asked to complete the Non-spontaneous Adverse Events Questionnaire either via RedCap or via an interview with study staff. This form will be completed for all breast cancer survivor participants and will query the participant as to whether they have had any health and/or medical problems during the preceding 8 week period. Participants will be called or emailed until a response is received. Participants will also be required to provide the investigators with at least one emergency contact to have on file in the event we are fail to reach the participant after 5 or more attempts. If participant reports “YES” to item 5A-5D (see RedCap form), an adverse event form will be filed with the IRB. The non-spontaneous Adverse Events Questionnaire will not be given to buddies of BCS participants to complete since they are not being specifically asked or encouraged to increase their physical activity participaiton.

All identified adverse events will be reported to the PI and recorded and reported in an adverse event log (includes subject’s name, date and event description). The PI will consult with co-investigators, the IRB and NU Office for the Protection of Research Subjects to determine whether the event should be classified as ‘non-attributable’, ‘possibly attributable’ or ‘attributable’ to the current project and ‘serious’ or ‘non-serious.’ Adverse event reports will be submitted to the IRB within 5 business days of the event or notification to the PI that the event has occurred. All serious adverse events will be reported to the RHLCCC Clinical Research Office for review by the Data Monitoring

Committee, IRB, and the National Cancer Institute, as applicable, using appropriate forms. Any action to be taken will be recorded in the adverse event log.

An adverse events is defined as an unanticipated problem which meets all of the following criteria: a) unexpected (in terms of nature, severity, or frequency) given the research procedures described in protocol-related documents and the characteristics of the subject population being studied, b) related or possibly related to participation in the research and c) suggests that the research places subjects or others at a different or greater risk of harm than was previously known or recognized. A 'serious' adverse event is defined as any event in which the outcome results in any of the following: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization (for > 24 hours), a persistent or significant disability/ incapacity or substantial disruption of the ability to conduct normal life functions; a congenital anomaly or birth defect; important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed, above. All other events will be considered 'non-serious.'

In addition to reporting any events as they occur to the IRB, a progress report and request for IRB renewal will be submitted the Northwestern University IRB annually. All non-serious adverse events will also be submitted to the RHLCCC Clinical Research office semi-annually. Furthermore, study progress reports will be submitted to the RHLCCC Clinical Research Office Data Monitoring Committee semi-annually. These reports will include accrual, withdrawals, reported adverse events and compliance issues.

9.3 *Procedures performed to lessen the probability or magnitude of risks.*

Phase 1. All participants will be informed during screening and in their informed consent with respect to how much time interviews, and/or app development will involve. All interviews and telephone/web-based app development sessions and interviews will be digitally recorded when possible; digital files will be stored on a password-secured network drive. Recordings will be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study. For intervention development, each participant will be randomly assigned an identification number to ensure confidentiality of data. All raw data will be de-identified and kept confidential.

Although, the purpose of this field test is NOT to test how well it works to increase physical activity, but rather to evaluate the app's functioning and ease of use in everyday life and participants will be explicitly told NOT to change their PA behavior and that the data they enter does not have to be accurate, we do recognize that some individuals may still attempt to increase their PA and to accurately respond to questions/prompts. Thus, we will follow the same procedures detailed, below, for Phase 2.

Electronic versions of all data will be kept on a password protected network with access limited to study investigators. Only the investigators will have access to participant data. Confidentially will be further maintained by reporting only group level data in study publications and presentations. All staff with access to the data with have completed

Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules.

Phase 2. All participants will be informed during screening and in their informed consent with respect to how much time the program, questionnaire completion, and all testing will involve. In addition, they will also be informed of the risks associated with participating in an exercise program. Survivors and buddies will be informed that participation is completely voluntary and they can discontinue at any point. They will also be provided with the option "I prefer not to answer" for every question in the study so they can opt-out of answering any questions for which they do not want to share responses or which make them uncomfortable.

Breast cancer survivors will be provided with an exercise prescription to progress safely through the program to minimize risk (see Table 5). All participants will be able to contact study investigators at any point by phone, e-mail or messaging through the app should they have any concerns regarding participation.

Table 5. *Fit2Thrive* Exercise Prescription

Week	Weekly Goal (Mins)	# Sessions Per Week	Session Duration (Mins)	Session RPE	Session Target Heart Rate (% Max HR)
1	30	2-3	10-15	10-12	50-60%
2	45	2-3	15-20	10-12	50-60%
3	60	3	20	10-12	50-60%
4	75	3	25	10-12	50-60%
5	90	3	30	10-12	50-60%
6	105	3	35	10-12	50-60%
7	120	3-4	30-40	10-12	50-60%
8	135	3-4	30-45	13-15	60-75%
9	150+	3-5	30-60	13-15	60-75%
10	150+	3-5	30-60	13-15	60-75%
11	150+	3-5	30-60	13-15	60-75%
12	150+	3-5	30-60	13-15	60-75%
13-24	150+	3-5	30-60	13-15	60-75%
RPE= Rating of Perceived Exertions; HR= Heart Rate					

Each participant will be randomly assigned an identification number to ensure confidentiality of data. RedCap does require an e-mail address to send the patient reported outcome measure links to participants and thus, data will be temporarily linked to individuals' e-mail addresses and first names which may be included in the e-mail for personalization purposes. However, these links will be removed when questionnaire data is downloaded and this data will then only be linked to the participant's identification number. Nitro Study Tracker, NOTIS and the study RedCap tracking database are the only places where the identification number and the participant's name will appear together in the present study and will only be accessible by the investigators.

For post-intervention interviews, all participants will be informed during screening and in their informed consent with respect to how much time interviews will involve. All interviews will be digitally recorded when possible; digital files will be stored on a password-secured network drive. Recordings will be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study.

All raw data will be de-identified and kept confidential. Electronic versions of all data will be kept on a password protected network with access limited to study investigators. Only the investigators will have access to participant data. Confidentially will be further maintained by reporting only group level data in study publications and presentations. All staff with access to the data with have completed Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules.

9.4 Study Measures.

A. Phase 1

Interviews

- Questions for the interviews are included in the Appendix. Questions will be related to their perceptions of specific intervention/app components, recommendations for features, changes or enhancements.

App Development Session 1 Survey

- This survey asks participants about their preferences and opinions regarding app features to assist in app development and design. Participants will also provide opinions on images/wireframes of potential app features.

Post-Field Test Survey for Individuals Given the App to Test:

- Participants will provide information on:
    - Learnability: Ease and time to learn system
    - Effectiveness: System's ability to promote performance and productivity
    - Efficiency: System's ability to improve speed at which they perform
    - Errors: Impact of errors on using system and ability to recover from errors
    - Flexibility: System's ability to provide different command or routes to achieve same goal
    - Memorability: Ability to remember how to use system next time and ability to re-learn system after periods of non-use
    - User Satisfaction: Fondness, perceptions and opinion of system and its features

App Notifications Field Test Survey (Wave 2 Field Test)

- Participants will be asked to rate app notification message content and provide any additional feedback for improving messages.

B. Phase 2

Primary Outcome Measures

Feasibility: This will be measured during the intervention, immediately post-intervention and after the follow-up period. Measures include:

- *Intervention reach*: # of participants enrolled/# of eligible individuals

- Participant retention: # of participants who drop out/# of participants randomized
- *Intervention Adherence*: % of weeks adhered to exercise prescription during intervention period
- *Intervention Maintenance*: % of weeks adhered to exercise prescription during follow-up period
- *Intervention component engagement:*
    - During intervention: # of times, on average, participants interacted with each intervention component during intervention
    - During follow-up: # of times, on average, participants interacted with each intervention component during follow-up
    - Total: # of times, on average, participants interacted with each intervention component over intervention and follow-up

Acceptability: This will be measured via a process evaluation immediately post-intervention and after the follow-up period. This evaluation will assess the following:

- perceived effectiveness of intervention components/app; use of app/intervention materials; plans to continue PA/app use; elements of intervention liked/disliked; satisfaction with program delivery, assessments and staff

Screening

Physical Activity Readiness Questionnaire (PAR-Q).[96] This pre-screening questionnaire assesses cardiovascular disease history, symptoms, risk factors and other health issues. Women indicating ≥1 positive statements will be required to obtain medical clearance from their primary care physician or oncologist.

Other Measures

All measures will be used for both breast cancer survivor participants and buddies unless otherwise indicated. Assessment will be conducted at baseline, 3 weeks (survivors only), 12 weeks and 24 weeks.

Mobile Device Proficiency Questionnaire.[98] This survey assess both assessing both basic and advanced proficiencies related to smartphone and tablet use across eight subscales: (a) Mobile Device Basics, (b) Communication, (c) Data and File Storage, (d) Internet, (e) Calendar, (f) Entertainment, (g) Privacy, and (h) Troubleshooting and Software Management.

Demographics. Data will be collected on participant's current age, race, ethnicity, employment status, number of children, education, marital status, income, height and weight.

Breast Cancer History. Participants will be asked to indicate their current menopausal status and provide details on the prior breast cancer diagnosis including: date of diagnosis, stage of disease, treatment type and duration and hormone receptor status. Women will be asked to indicate similar data for any cancer recurrences or second

cancer diagnoses. **This measure will only be used for breast cancer survivor participants.**

Health History. Participants will be asked to rate their general, overall health status, indicate whether they have been diagnosed with a list of 20 chronic conditions including diabetes, heart disease, multiple sclerosis, depression, etc. and provide information of other general health behaviors (e.g. smoking, drinking, fruit and vegetable consumption, etc.). **A slightly different version to capture potential cancer diagnoses will be used for buddy participants.**

Godin Leisure Time Exercise Questionnaire (GLTEQ).[99] The GLTEQ is a simple, self-administered instrument that has been widely used in epidemiological, clinical, and behavioral change studies and has been shown to be both a valid and reliable measure of PA participation. Participants will be asked indicate the frequency and average amount of time they spent engaging in strenuous (e.g., jogging), moderate (e.g., fast walking), and mild (e.g., easy walking) exercise over the past seven days. Weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. These values are added to obtain a total leisure activity score. Test-retest reliability coefficient range from r=0.48 for light and moderate activity to 0.94 for strenuous. For total values the test-retest reliability coefficient is 0.74.[99] **Breast cancer survivors will also answer a modified version asking them about their PA *before diagnosis* at baseline.**

Actigraph Accelerometer (model wGT3X-BT, Health One Technology, Fort Walton Beach, FL). The Actigraph is a valid and reliable objective PA measure.[100,101] It is small, lightweight, has a rechargeable battery that lasts for up to 25 days and provides no feedback to participants. Participants will be instructed to wear the monitor on the non-dominant hip during all waking hours for 7 consecutive days, except when bathing or swimming. Activity data will be collected in one-minute intervals (epochs). Participants will record any time the accelerometer was not worn on a log. The ActiLife software will be used to derive wear time, identify outliers and summarize daily variables of the minute-by-minute data. Non-wear time will be defined as intervals of at least 60 consecutive minutes of zero counts, with allowance for up to 2 minutes of observations of less than 100 counts/min within the non-wear interval.[102]A valid day of accelerometer wear will be defined as ≥10 hours of wear time. Each valid minute of wear time will be classified according to intensity (counts/min) using commonly accepted activity count cut-points [102,103] as follows: sedentary (<100), light activity (100-759), lifestyle activity (760-2019), and MVPA (≥ 2020). **This measure will only be used for breast cancer survivor participants.**

Sitting Time Questionnaire.[104] Women will be asked to indicate the amount of time they spend on a typical weekday and weekend sitting in the following activities: traveling to and from places, while at work, while watching television, while using a computer at home in leisure time NOT including television (e.g. visiting friends, movies, dining out, etc.). Test-retest reliability coefficients were high for weekday sitting time at work,

watching television and using a computer at home (r_s=0.78-0.84) but are more variable for weekend days across all domains (r_s=0.23-0.74).[104]

PROMIS Applied Cognition-General Concerns Short Form 8a.[105] The PROMIS Applied Cognition General Concerns Short Form 8a will be used to assess participants' frequency of perceived cognitive function over the past 7 days ranging from 1 (not at all) to 5 (very often). Higher scores reflect higher levels of cognitive concerns. The reliability of this measure ranges from α=0.90 to α=0.95.[106]

PROMIS Physical Function Short Form 20a.[105] The PROMIS Physical Function Short Form 20a will be used to assess participants' physical function. The scale has two subscale limitations and interference. For the 6 limitations items, participants will rate the level of difficulty they have had executing discrete activities over the past 7 days on a scale from 1 (unable to do) to 5 (without any difficulty). For the 4 limitations items, patients will rate the degree to which their health limits them in specific activities on a scale from 1 (cannot do) to 5 (not at all). Higher scores reflect better physical function. The reliability of this measure ranges from α=0.90 to α=0.95.[106]

PROMIS Fatigue Short Form 8a.[105] The PROMIS Fatigue Short Form 8a will be used to assess participants' frequency of fatigue symptoms ranging from 1 (not at all) to 5 (very much) and fatigue interference ranging from 1 (never) to 5 (always) over the past 7 days. Higher scores reflect higher levels of fatigue. The reliability of this measure ranges from α=0.90 to α=0.95.[106]

PROMIS Sleep Disturbance Short Form 8a.[105] The PROMIS Sleep Disturbance Short Form 8a will be used to assess participants' rating of overall sleep quality from 1 (very good) to 5 (very poor) and perceptions of specific characteristics of sleep quality on a scale ranging from 1 (not at all) to 5 (very much). Higher scores reflect higher levels of sleep disturbance. The reliability of this measure ranges from α=0.90 to α=0.95.[106]

PROMIS Depression Short Form 8a.[105] Participants are asked to indicate the frequency of a variety of depressive symptoms over the past 7 days on a 5 point scale from 1 (never) to 5 (always). Higher scores reflect higher depressive symptoms. The reliability of this measures ranges from α=0.90 to α=0.95.[106]

PROMIS Sleep-Related Impairment Short Form 8a. [105] The PROMIS Sleep –Related Impairment Disturbance Short Form 8a will be used to assess participants' perceptions or sleep-related impairment on a scale ranging from 1 (not at all) to 5 (very much). Higher scores reflect higher levels of sleep-related impairment. The reliability of this measure ranges from α=0.90 to α=0.95.[106]

Physical Activity Neighborhood Environment Survey.[107] Participants are asked to indicate the different facilities and features of the area around their home that they could walk or bike. The items on this measure have demonstrated test-retest interclass correlations ranging from 0.52 to 0.88 and spearman correlations between single items

and similar subscales from a more detailed measure were significant and ranged from 0.27 to 0.81.[107]

Exercise Self-efficacy Scale.[108] The 6-item Exercise Self-Efficacy Scale will be used to assess participants' beliefs in their ability to exercise five times per week, at a moderate intensity, for 30 or more minutes per session at two week increments over the next 12 weeks. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). The internal consistency for this measure has demonstrated acceptability (α=0.90).[108]

Barriers Self-efficacy Scale.[108] The 15-item Barriers Self-Efficacy Scale will be used to assess participants' beliefs in their ability to exercise three times per week for the next 3 months in the face of commonly experiences barriers to activity. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). The internal consistency for this measure has demonstrated acceptability (α=0.86).[108]

Social Support for Exercise Scale.[109] This scale assesses the degree to which friends and family have demonstrated support for exercise behaviors in the previous 3 months. The frequency for each item is rated once for both family and friends on a 5-point Likert scale, ranging from 1 (never) to 5 (very often). The friend and family subscales have demonstrated acceptable internal consistency (α=0.84 and α=0.84, respectively). [109]

Effective Social Support for Physical Activity.[110] This scale assesses perceptions of support given (for buddy) and received (for BCS). The scale assesses three different types of help or support: 1) Help with practical needs, 2) Advice or information, and 3) Emotional support. **There will be a separate version for Buddies and breast cancer survivor participants assigned to the buddy condition only.**

Exercise Goal-setting Scale.[111] This 10-item scale will assess participants exercise-related goal-setting, self-monitoring and problem solving and instructs participants to indicate the extent to which each of the statements describes them on a scale from 1 (does not describe) to 6 (describes completely). This scale has demonstrated good internal consistency (α= 0.89). [111]

Multidimensional Outcome Expectations for Exercise Scale.[112] This scale will assess participants' social (4 items), self-evaluative (5 items), and physical (6 items) outcome expectations for exercise participation on a 5 point scale ranging from 1 (strongly disagree) to 5 (strongly agree). The three subscales have demonstrated good internal consistency (α= 0.82 for physical outcome expectations, α= 0.81 for social outcome expectations, and α= 0.84 for self-evaluative outcome expectations).[112]

Physical Activity Enjoyment Scale.[113] This 18-item scale will assess the degree to which participants, at the current moment, enjoy doing any sort of physical activity. This 18-item scale rates enjoyment on a 7-point bipolar scale ("It makes me depressed"…"It makes me happy"). This measure has demonstrated good internal consistency in previous studies (α= 0.93 to α= 0.96).[113]

Table 6. Schedule of Measures					
	Screening	**Baseline**	**3 weeks**	**12 weeks**	**24 weeks**
Physical Activity Readiness Questionnaire	**X**				
Mobile Device Proficiency Questionnaire		**X**			
Demographics		**X**			
Breast Cancer History		X		X	X
Health History		**X**		**X**	**X**
Actigraph Accelerometer		X		X	X
Godin Leisure Time Exercise Questionnaire-Current		**X**	X	**X**	**X**
Godin Leisure Time Exercise Questionnaire-Before diagnosis		X			
Sitting Time Questionnaire		**X**		**X**	**X**
PROMIS Physical Function Short Form 20a		**X**		**X**	**X**
PROMIS Fatigue Short Form 8a		**X**		**X**	**X**
PROMIS Depression Short Form 8a		**X**		**X**	**X**
PROMIS Anxiety Short Form 8a		**X**		**X**	**X**
PROMIS Emotional Support Short Form 8a		**X**		**X**	**X**
PROMIS Sleep Disturbance Short Form 8a		**X**		**X**	**X**
PROMIS Sleep-Related Impairment Short Form 8a		**X**		**X**	**X**
Rosenberg Self-Esteem Scale		**X**		**X**	**X**
Physical Self-Perception Profile Physical Self-worth Subscale		**X**		**X**	**X**
Physical Activity Neighborhood Environment Survey		**X**			
Exercise Self-efficacy Scale		**X**	X	**X**	**X**
Barriers Self-efficacy Scale		**X**	X	**X**	**X**
Social Support for Exercise Scale		**X**	X	**X**	**X**
Effective Social Support for Physical Activity		***X***	*X*	***X***	***X***
Exercise Goal-setting Scale		**X**	X	**X**	**X**

Physical Activity Enjoyment Scale		**X**	X	**X**	**X**
Multidimensional Outcome Expectations for Exercise Scale		**X**	X	**X**	**X**
Post-Program Evaluation				**X**	**X**
*Values in bold indicate BOTH survivors and buddies will be asked to complete measure at a given time point. Italics indicate only survivors in buddy condition and buddies will complete.					

Post-intervention Interviews. Questions for the interviews are included in the Appendix. Questions will be related to their perceptions and opinions of the intervention, overall, and specific intervention/app components and recommendations for improving the intervention in the future.

10.0 Data and Specimen Banking

All data will be kept for 7 years after publication, as required by Northwestern University. Blood specimens will be banked in a freezer in the basement of 680 N Lake Shore Drive, Chicago, IL for future use. Specimens will not be stored linked to direct identifiers (only by randomly assigned participant identification number, as described below in data security section). The specimens will not be destroyed, and they will only be used in the future for research purposes. Specimens will be accessible by Dr. Phillips and co-investigators with IRB approval.

11.0 Data and Specimen Management

11.1 Data Analysis Plan.

Phase 1. Stakeholders will contribute to intervention component development via interviews which will be digitally recorded; digital files will be stored on a password-secured network drive. Recordings will be transcribed verbatim and de-identified. Three coders will independently review the de-identified transcripts, identify emergent themes, and assign initial codes using constant comparative analysis. This iterative process codes data based on identified conceptual themes. Data will be organized using NVivo software. Coders will meet often to discuss and refine the emerging themes, and triangulate their perspectives. Once a final coding structure is identified, coders will independently return to the transcripts to re-examine them and recode as necessary to ensure consistency. Disagreements will be resolved through deliberation and consensus. Analysis will identify the three stakeholder groups (survivors, experts, community organizations) perspectives on desirable components for inclusion. All groups' perceptions of components, how to implement the proposed intervention and strategies for tailoring intervention content, and tactics for overcoming challenges to implementation will be integrated. These components will be vetted via the Breast Cancer Survivor Stakeholder Advisory Board Session. After vetting from the advisory board, the final 5 components will be selected for development.

Once components to be tested are identified and the app is under development, usability testing will begin. For this, survivors will be given a defined set of tasks to complete. They

will be observed to determine the ease with which they navigate using various app functions (e.g. error rates, time to complete tasks, etc.). Survivors will also provide qualitative and quantitative feedback regarding features, ease of use, and likeability. Usability tests will be rapid and iterative. During the field testing period, design changes will be completed after receipt of 2 to 5 survivors' feedback and then tested with the next set of 2 to 5 survivors. The app will be refined to eliminate issues that impeded usability. We anticipate 10-20 survivors will be needed to achieve saturation on issues identified during testing. Following the field testing, they will participate in a session to provide feedback on the app features and functioning. Because consensus may be reached during the field testing before all participants have a chance to participate, survivors may or may not participate in the field testing and post-field testing sessions. Finally, survivors will participate in a final lab visit where they evaluate the close-to-final intervention and provide feedback.

Phase 2. The effects of the five individual intervention components will be examined by means of a factorial experiment (see Table 4 for an example). The final factors will be determined based on the findings from Phase 1 of the study. Although these components will be evidence-based and have been included in bundled PA interventions previously found to be successful, none of these prior studies were designed to estimate the impact of any individual component.

We chose a factorial experimental design factorial experiments have two characteristics essential to the success of MOST. These experiments: a) separate component effects enabling the estimation of the main effect contribution of each candidate component and interactions between components[114] and b) are more economical compared to alternative designs because they often require substantially fewer subjects to achieve the same power and use less resources .[114,115]

A complete factorial experiment requires 2^5=32 experimental conditions. It is important to understand that this design should not be considered a multiple arm RCT. All of the estimated main effects and interactions will be based on all experimental conditions. Table 7 displays the experimental conditions for this study. For example, main effect of telephone support calls would be estimated by comparing the mean of experimental conditions 1-7 with the mean of conditions 8-16. Similarly, the main effect of the App+ would be estimated by comparing conditions1-4 and 9-12 with conditions 5-8 and 13-16. Thus, all 256 participants will be included in all effect estimates.

Table 7. Experimental Conditions

Exp Condition	Support Calls	App+	Buddy	Online Gym	App Notifications
1	yes	no	no	no	no
2	yes	yes	no	no	no
3	yes	no	yes	no	no
4	yes	no	no	yes	no
5	yes	no	no	no	yes

6	no	yes	no	no	no
7	no	yes	yes	no	no
8	no	yes	no	yes	no
9	no	yes	no	no	yes
10	no	no	yes	no	no
11	no	no	yes	yes	no
12	no	no	yes	no	yes
13	no	no	no	yes	no
14	no	no	no	yes	yes
15	no	no	no	no	yes
16	yes	yes	yes	no	no
17	yes	yes	no	yes	no
18	yes	yes	no	no	yes
19	yes	no	yes	yes	no
20	yes	no	yes	no	yes
21	yes	no	no	yes	yes
22	no	yes	yes	yes	no
23	no	yes	yes	yes	yes
24	yes	no	yes	yes	yes
25	no	no	yes	yes	yes
26	no	yes	no	yes	yes
27	yes	yes	yes	yes	no
28	yes	yes	yes	no	yes
29	yes	yes	no	yes	yes
30	no	no	no	no	no
31	no	yes	yes	no	yes
32	yes	yes	yes	yes	yes

Planned analyses for each aim are as follows:

Aim 1. All individual interviews will be digitally recorded; digital files will be stored on a password-secured network drive. Recordings will be transcribed verbatim and de-identified. Three coders will independently review the de-identified transcripts, identify emergent themes, and assign initial codes using constant comparative analysis. This iterative process codes data based on identified conceptual themes. Data will be organized using NVivo software. Coders will meet often to discuss and refine the emerging themes, and triangulate their perspectives. Once a final coding structure is identified, coders will independently return to the transcripts to re-examine them and recode as necessary to ensure consistency. Disagreements will be resolved through deliberation and consensus. Analysis will identify both aides' and clients' perceptions of implementing the proposed intervention, strategies for tailoring the existing intervention content, and tactics for overcoming identified challenges to implementation.

All information obtained from direct observation with be entered and analyzed using descriptive statistics to determine the learnability, effectiveness, efficiency, errors, flexibility, memorability, and user satisfaction of the app components. We will also transcribe verbatim the de-identified digitally audio recorded files and use these data to further assess qualitatively any themes that emerge relative to the components' learnability, effectiveness, efficiency, errors, flexibility, memorability and user satisfaction. Finally, descriptive statistics (means, standard deviation, frequencies) of questionnaire-based feedback will be used to further assess the app's the learnability, effectiveness, efficiency, errors, flexibility, memorability and user satisfaction.

Data from participant interviews and questionnaires completed related to the field experiment will be analyzed as described, above, and used to refine the app until saturation is reached.

Aim 2. *Feasibility and acceptability will be evaluated using the measures detailed above. The primary hypotheses are: a) 75% of eligible survivors will agree to participate in the intervention; (b) enrollees will demonstrate engagement by monitoring PA on >80% of the study days and using one or more additional app components at least weekly. Descriptive analyses (means, frequencies) will be used to describe these results.* Data from post-intervention interviews will be digitally recorded; digital files will be stored on a password-secured network drive. Recordings will be transcribed verbatim and de-identified. Three coders will independently review the de-identified transcripts, identify emergent themes, and assign initial codes using constant comparative analysis. This iterative process codes data based on identified conceptual themes. Data will be organized using qualitative data analyses software. Coders will meet often to discuss and refine the emerging themes, and triangulate their perspectives. Once a final coding structure is identified, coders will independently return to the transcripts to re-examine them and recode as necessary to ensure consistency. Disagreements will be resolved through deliberation and consensus. Analysis will identify both aides' and clients' perceptions of implementing the proposed intervention, strategies for tailoring the existing intervention content, and tactics for overcoming identified challenges to implementation.

Aim 3 and Exploratory Aim 1. These aims are to determine the preliminary effectiveness of intervention components on minutes of accelerometer-measured moderate and vigorous PA (Aim 3) and PROs (physical function, fatigue, depression, QOL; Exploratory Aim). Our hypothesis is that a set of components will emerge as most effective for increasing PA and minimizing cost, but a second set of intervention component may emerge as having the largest, most cost-efficient impact on PROs. These hypotheses will be tested using intention-to-treat mixed linear model analyses to test differences in outcomes by intervention components. The study was not designed to have statistical power to detect differences over time with inferential tests. If descriptive statistics suggest that the intervention (a) is feasible and acceptable and (b) seems likely to increase PA, we will plan a future randomized controlled trial with sufficient power (>.80) to detect clinically-meaningful effects in this population. If we fail to achieve certain benchmarks for

feasibility, acceptability, or safety, we will refine the protocol as needed prior to proceeding.

Exploratory Aim 2. This aim is to explore the relationship between the 5 intervention components and each BC progression (IL-6, IL-10, CRP and TNFα) and cardiometabolic (CRP, BG, TG, TC, HDL-C) biomarker. We will also examine effects on overall risk for each category using composite z-scores. Our hypothesis is a set of components will emerge as most effective for changing each biomarker, but a second set of components, which may not be the same, may emerge as having the greatest composite effect or being most cost-efficient to achieve these outcomes. We will employ an intention-to-treat (ITT) approach by including all participants recruited into the study regardless of compliance. These hypotheses will be tested using intention-to-treat linear mixed model analyses to test differences in outcomes by intervention components. We will also test 2-way interactions between selected intervention components. Because we will use effect (-1,1) coding rather than dummy (0,1) coding, the power for tests to detect main effects and interaction effects are identical for effects of identical size. These data will be used in conjunction with parent study data to determine which intervention components will be tested in a more definitive trial.

11.2 Power Analysis.

Because this is a pilot test to evaluate the feasibility, acceptability, and preliminary efficacy of the different intervention components, sample size planning was determined by resource constraints (vs. a power analysis) for the primary aims.

Dried Blood Spots. To determine if the sample size (n=256) is sufficient to address our exploratory aim to explore biomarkers obtained via DBS, we conducted a power analysis to calculate the minimal detectable difference (MDD)[116] for each biomarker assuming 20% attrition at 24 weeks, an alpha of 0.05, and two-sided testing. The MDD defines the difference that must exist between those with the component "on" vs. "off" to detect a statistically significant effect. We used standard deviations from published BCS PA interventions[117] and intra-class correlations (ICC) from Dr. Spring's prior study,[118] if available. Otherwise, a conservative ICC of 0.8 is assumed. Table 8 displays MDDs for component main effects and two-way interactions at 12 and 24 weeks. We have 80% power to detect differences at least equal to between group differences observed in prior intervention studies for all inflammatory[119,120] and CVD markers[121,122] except for BG. Given no study has evaluated specific PA intervention component effects on biomarkers in BCS in the context of a MOST design, we accept this limitation.

Table 8. Minimal Detectable Differences

Marker	SD	ICC	Study	MDD
IL-6	1.1	0.80	Jones 2013	**0.40 pg/mL**
IL-10	3.8	0.80	Rogers 2012	**1.37 pg/mL**
TNFα	0.6	0.80	Jones 2013	**0.21 pg/mL**
CRP	2.4	0.44	Jones 2013	**0.78 mg/dL**
BG	7.8	0.49	Guinan 2013	2.57 mg/dL
HDL-C	0.3	0.87	Fairey 2005	**0.11 mmol/L**
TG	0.7	0.79	Fairey 2005	**0.27 mmol/L**
TC	0.3	0.75	Fairey 2005	**0.10 mmol/L**

11.3 Data Security

Each participant will be randomly assigned an identification number to ensure confidentiality of data. This will be the only way of matching data with a specific person. Nitro Study Tracker will be the only place where the ID will appear with the participant's name in the present study. This database will only be accessible by the investigators.

This electronic database will house participant contact information and is stored on a secured, password-protected network, accessible only by the investigators.

To ensure the integrity of the data collected from study participants several procedures will be implemented. All personnel involved in data collection will be thoroughly trained in all assessment methods thus ensuring consistent applications of procedures and measurement consistency across participants. All data will be automatically saved in the secured, password protected RedCap system and will be downloaded to a password protected network folder protected ensuring access only by the investigators. Any hard copies of data will only include the participants ID number and will be entered into the RedCap system only using this ID number. All raw data will be de-identified (with the exception of the study ID number). These data will be saved to a portable hard drive which will be stored in a locked cabinet in the PI's laboratory. Any hard copies of data will be stored in a separate, locked cabinet from the informed consents in the PI's laboratory. Files containing identifying information obtained for purposes of tracking participants and monitoring of subject payments are kept in a locked file in a locked office separate from study related data. Data will only be linked to identifying information through a study ID. Under no circumstances will individually identifiable data be released to anyone without the written consent of the subject. Results will be reported as group findings only. In the past we have found that all of these procedures are effective at reducing risk for study participants.

Issues related to data integrity will be discussed on a weekly basis as a recurring agenda item in the weekly project meeting to ensure constant monitoring of our data integrity. Only the investigators will have access to participant data. All staff with access to the data with have completed Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules.

11.4 Quality Control of Collected Data

Given that the majority of data will either be recorded electronically, entered electronically by participants or collected electronically via accelerometers or cellphones, we anticipate limited issues with quality control. However, all hard copy data that is entered by study staff will be double entered and checked to ensure data integrity Additionally, all data will be checked for missing data and erroneous data by examining descriptive statistics and score ranges of all variables. Subsequently, all data will be examined for violation of basic statistical assumptions (i.e., normality, multicollinearity, and homoscedascity) and transformed if necessary. In order to ensure data are missing at random, we will compare participants who have data on a given variable to those who do not on demographic and disease characteristics to ensure there is no pattern to the missingness.

11.5 Specimen Handling

Blood specimens will be self-collected by participants in their homes and mailed back to 680 N Lake Shore Drive, Chicago, IL using the U.S. Postal Service for analysis and storage for future use which may include analysis of biomarkers of BC progression and CVD risk, whole genome sequencing, and epigenetic profiling. Everyone handling the blood products will receive Bloodborne Pathogens Training. As described above,

specimens will not be stored linked to direct identifiers (only by ID number). Specimens will be accessible by Dr. Phillips and co-investigators with IRB approval.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

N/A as this study involves only Minimal Risk to subjects.

13.0 Withdrawal of Subjects

13.1 Procedures for early termination.

Participants may withdraw from either Phase 1 or Phase 2 of the study at any time.

Procedures specific to Phase 2. For any participant who elects to withdraw, permission will be sought to continue to collect outcome data for use in the analysis. However, all participants in the intervention will be accounted for in all follow-up analyses following the intent-to-treat principle. If participants withdraw from the study, and do not agree to return for follow-up assessments, data from their most recent assessment will be carried forward and imputed in subsequent assessment points (Last Observation Carried Forward).

13.2 Procedures to follow when subjects withdraw from research.

Participants may withdraw from the study at any time during Phase 1 or Phase 2. For phase 2, permission will be sought to continue to collect outcome data for use in the analysis.

14.0 Risks to Subjects

14.1 Reasonably foreseeable risks, discomforts, hazards, or inconveniences related to participation in the research.

Phase 1. Potential risks are considered minimal. There are some potential minimal psychological risks associated with participation in the interviews, intervention development sessions and answering some of the intervention development questionnaires. However, participants will be given the option to not answer or skip any questions that make them feel uncomfortable. Further, although the research team will take every precaution to maintain confidentiality of the data, the nature of some web-based sessions prevent the researchers from guaranteeing confidentiality. The research team will be sure to reiterate this risk during all group sessions and remind participants to respect the privacy of your fellow participants and not repeat what is said in these sessions to others.

For the app field study, participants may increase their PA compared to their usual level of PA, although they will be explicitly told this is not the purpose of the field test. Engaging in a PA program when one has been sedentary for a considerable period of time incurs some risk of injury such as l muscle soreness, strains, aggravation of arthritic conditions, etc. However, serious physical injury is considered unlikely. Participants will be instructed to notify study investigators immediately if they experience any adverse effects of using the app.

For the app field study, there is also a small risk to individuals' privacy when using the mHealth app. However, this will be minimized by the procedures described, above. Participants are permitted to refuse to participate in any aspect of the research and may withdraw from the study at any point, for any reason without penalty.

Phase 2. Potential risks are considered minimal. Engaging in a PA program when one has been sedentary for a considerable period of time incurs some risk of injury such as l muscle soreness, strains, aggravation of arthritic conditions, etc. However, serious physical injury is considered unlikely. In order to reduce and/or prevent any physical harm or injury subjects will gradually increase their PA. Additionally, each participant will be required to pass a screening test or receive medical approval prior to enrollment to ensure PA is appropriate. Furthermore, all participants, regardless of the intervention components they receive, will be provided access to a study website that is also embedded within the app which will include an overview of safety issues and stress the need to contact study investigators should they experience any adverse effects of PA. Finally, the intervention content will emphasize safety and present instruction to reflect safe progressions.

In addition to the potential minimal risk associated with PA participation, there are some potential minimal psychological risks associated with answering some of the questionnaires required for participation in this study. However, participants will be given the option to skip any questions that make them feel uncomfortable. Should any individuals report scores on the PROMIS Cancer Depression Scale, that are in the 75th percentile (i.e. ≥ 4.3) or confer a high level of distress in interactions with research study staff, they will be referred to American Psychosocial Oncology Society (APOS) Toll-Free HELPLINE - 1-866-276-7443 (1-866-APOS-4-HELP). We have chosen this method because women will be selected from all over the United States. APOS's Helpline is a national resource to help people with cancer and their caregivers find emotional support in their own communities. This is a referral program that is part of the Cancer Support Helpline® (affiliated with the Cancer Support Community) and connects cancer patients, their caregivers and advocacy organizations with psychiatrists, psychologists, nurses, social workers, and counselors skilled in the management of cancer-related distress. If Helpline counselors cannot find local support services, and there is an immediate need for help, a Helpline mental health counselor can provide short-term emotional support by phone while patients seek professional help with coping in their community. Calls are accepted Mon-Fri 9 am- 8 pm ET.

There is also a small risk to individuals' privacy when using the mHealth app but this will be minimized by the procedures described, above.

Finally, for those participating in the optional blood sample collection, pricking the finger for the blood sample may cause some minor discomfort. Additionally, the risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the collection site and infection, and a rare risk of fainting. The risk of fainting could be elevated if a participant is already feeling faint or dizzy. They will be instructed to delay collecting the blood sample until they are feeling better if this is the case.

Participants are permitted to refuse to participate in any aspect of the research and may withdraw from the study at any point, for any reason without penalty.

15.0 Potential Benefits to Subjects

Phase 1. The benefits of this portion of the study are largely scientific. Participants will have the benefit of contributing to the advancement of science by contributing to the development of a mHealth intervention for breast cancer survivors. This information is crucial to the effective development and implementation of the PA intervention to be tested in Phase 2.

Phase 2. Although not guaranteed, the potential benefits of participating in this study include improved cardiorespiratory fitness, physical functioning, quality of life, depression and fatigue. All participants will be able to participate in the program for free. This study has the potential to inform science by improving the understanding of how to promote PA in breast cancer survivors, a large, and growing population with many health concerns. Additionally, the approach used to develop the intervention has the potential to be applied to other areas of science to facilitate the efficiency by which research can be disseminated into practice. We believe that the minimal risk involved with study participation are reasonable in relation to the anticipated benefits.

16.0 Vulnerable Populations

N/A

17.0 Community-Based Participatory Research

17.1 Involvement of the community in the design and conduct of the research.

Stakeholders including local, Chicago-area breast cancer survivors and representatives from relevant Chicago-area and national cancer organizations will be involved in designing and choosing the intervention components to be tested as part of Phase 1 of this study.

18.0 Sharing of Results with Subjects

Phase 1. Women who participate in this portion of the study will have the option of selecting to receive a plain language study summary at the end of Phase 1 and to indicate whether they would like to receive any manuscripts that result from Phase 1 or Phase 2 of the present study. All women who indicate they would like to receive either the plain language summary or have manuscripts shared with them, will be e-mailed final versions of any manuscripts that result from the data upon publication in peer-reviewed journals. These manuscripts will also be posted on the PI's website which study participants will have access to.

Phase 2. Results will be shared with subjects via a plain-language study summary that will be sent via e-mail to participants at the conclusion of all data collection and cleaning. Women will also be given the option to indicate they would like manuscripts that are

published as a result of these data to be shared with them. All women who indicate they would like to have manuscripts shared with them, will be e-mailed final versions of any manuscripts that results from the data upon publication in peer-reviewed journals. These manuscripts will also be posted on the PI's website which study participants will have access to.

19.0 Setting

19.1 Sites or locations where research will be conducted.

Phase 1. Recruitment. Breast cancer survivors will be recruited from the Lynn Sage Breast Cancer Program at RHLCC using pamphlets/fliers and physician referrals. Fliers and pamphlets will also be posted in the local community, sent to listservs and posted on social media and on-line forums. Additionally, the PI will send a recruitment e-mail to an existing database of breast cancer survivors. Community representatives will be recruited in conjunction with NU's Center for Community Health (led by Co-I Dr. Ackermann) via personalized e-mails and phone calls. Experts will be recruited through the RHLCCC and the PI's, co-investigators' professional networks via listservs and personalized e-mails and phone calls. Research Procedures: All research procedures will be performed in the Department of Preventive Medicine, 680 N. Lakeshore Drive, Suite 1400, Chicago, IL 60611.

Phase 2. Recruitment: Our main source of recruitment will be e-blasts sent to women registered with the Army of Women.© Other recruitment sources will include posting on on-line forums and websites, RHLCC, and fliers distributed at local community organizations and events. Research Procedures: All research procedures will be performed in the Department of Preventive Medicine, 680 N. Lakeshore Drive, Suite 1400, Chicago, IL 60611.

20.0 Resources Available

20.1 Qualifications PI and staff

All staff with access to the data with have completed Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules. The PI (Dr. Phillips) is an Assistant Professor in the Department of Preventive Medicine and has a PhD in Kinesiology from the University of Illinois Urbana Champaign, MPH in Quantitative Methods from Harvard University and completed a postdoc at the National Cancer Institute. She has extensive training in randomized physical activity intervention in cancer survivors and older adults and has successfully conducted several other, similar, studies while at the University of Illinois Urbana Champaign.

Co-Investigators. Dr. Bonnie J. Spring, PhD is the Director of The Center for Behavior and Health and Professor in Preventive Medicine, and Co-Leader of the Cancer Prevention Program at RHLCC at NU. Dr. Spring has extensive experience in mHealth, behavioral intervention trials and MOST methodology. Dr. Frank J. Penedo, PhD is the

Director of the Cancer Survivorship Institute at RHLCC, Program Leader of Cancer Control and Survivorship at the RHLCC, and Professor in Medical Social Sciences at NU. D. Penedo has extensive experience in behavioral interventions in cancer survivors and biopsychosocial mechanisms underlying health and disease outcomes in cancer survivors. Dr. David Cella, PhD is the Chair of the Department of Medical Social Sciences and Director of the Center for Patient-Centered Outcomes at NU. He is a leading expert in cancer survivorship and patient reported outcomes. He also has experience in designing and conducting stakeholder focus groups and interviews. Dr. Ronald T. Ackerman, MD, MPH is the Director of the Center for Community Health and Professor in General Internal Medicine and Geriatrics. He is an expert in dissemination and implementation of behavioral interventions and stakeholder engagement. Dr. Juned Siddique, PhD is an Associate Professor in Biostatistics and Preventive Medicine and an expert in using cutting-edge statistical techniques to analyze behavioral interventions and accelerometer data. Dr. Danielle Hartigan, PhD, MPH is an Assistant Professor at Bentley University in Natural and Applied Sciences. She has expertise in qualitative data collection and analyses and will provide guidance on these aspects of the study.

20.2 Other resources available to conduct the research.

Feasibility of recruiting subjects for Phase 1. We will use the Army of Women© to recruit survivors. Given the large number of survivors in the database and the fact that no on-site lab visits are required, we do not anticipate recruitment to be a problem. We believe we should be able to recruit participants for the other stakeholder groups relatively easily through NU resources including RHLCC and the Center for Community Health in addition to the PI's and Co-I's professional networks.

Feasibility of recruiting subjects for Phase 2. Women will primarily be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history. This means we only need to recruit (0.2%) of these women.

We are confident sample recruitment through the Army of Women© is feasible, based on my prior experience recruiting and retaining a much larger sample. In our prior study, we had 2,500 women express interest within 12 hours of recruitment initiation and recruitment was halted due to capacity limitations. Of that number, 1,631 (64%) responded to screening and qualified to participate. I randomized 500 of those women to wear accelerometers for 7 consecutive days. Only 4 refused to wear the device. At baseline and follow-up, 1,527 women (94%) completed more than half of the on-line questionnaires. Valid accelerometer data were obtained from 442 (89%) women at baseline; 370 (83.7%) of those women also had valid data at 6 month follow-up. Reasons for missing accelerometer data at baseline and follow-up, respectively, were: did not wear (n=36 and n=40), insufficient valid wear time (n=8 and n=17), accelerometer malfunctioned (n=5 at both), lost in mail or by participant (n=4 and n=5) and submerged in water (n=1).

If we are not able to sufficiently meet our recruitment goals using the Army of Women©, additional NU resources (e.g. RHLCC and the Center for Community Health), on-line

forums and social media sites (i.e. Facebook, the Sisters Network and Nueva Vida) and fliers at community organizations and events will be used.

Percentage of PI's Effort Dedicated to Project. The PI will dedicate approximately 60-80% of her effort to this project during data collection and between 30-40% during data analyses.

Facilities. Phase 1 will be conducted in the Department of Preventive Medicine in private conference rooms or using the Northwestern University's IT services (for web-based conferences). Phase 2 will be conducted via a mobile app. All data from this will be stored on a secure, password protected server that will only be accessible to study investigators.

Process to Ensure all Staff are Adequately Informed on Protocol. All staff with access to the data with have completed Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules. A manual of procedures will be developed for the current project which will include scripts for any contact research staff will have with study participants. The PI will meet with the research assistant (TBD) from the Department of Preventive Medicine to train them in these procedures. Additionally, the PI will meet with the RA on a weekly basis, and as needed, to ensure study procedures are being adhered to.

21.0 Prior Approvals

We will obtain approval from the National Cancer Institute before beginning the present study.

22.0 Recruitment Methods

22.1 When, where and how potential subjects will be recruited.

Phase 1. Women will be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study investigator who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent. Breast cancer survivors may also be recruited from the Lynn Sage Breast Cancer Program at RHLCC using pamphlets/fliers and physician referrals. Fliers and pamphlets will also be posted in the local community sent to listservs and posted on social media and on-line forums. Additionally, the PI will send a recruitment e-mail to an existing database of breast cancer survivors. Community representatives will be recruited in conjunction with NU's Center for Community Health (led by Co-I Dr. Ackermann) via personalized e-mails and phone calls. Experts will be recruited through the RHLCCC and the PI's, co-investigators' professional networks via listservs and personalized e-mails and phone calls.

All individuals interested in participants will be instructed to contact study investigators who will provide a description of the study and further screen for eligibility either via on-

line screening questionnaires or telephone interview. Eligible stakeholders will be offered the opportunity to participate and will complete informed consent.

Phase 2. Breast cancer survivors will be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study investigator who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

If our recruitment goals are not being sufficiently met via the Army of Women© we will also post study fliers and advertisements on social media sites (i.e. Facebook, PatientsLikeMe) and on-line forums (i.e. Sisters Network, Nueva Vida, Living Beyond Breast Cancer). All women who are recruited through these alternative strategies, will be instructed to contact the study staff who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

Buddies will be identified by participants and subsequently contacted by investigators via email. Identified potential buddies will have access to an online screening tool via RedCap which will provide a study overview and allow them to screen for eligibility if interested. Eligible buddies will be offered the opportunity to participate and will complete informed consent. They will also be offered the opportunity to answer an online questionnaire battery that is almost identical to that of the breast cancer survivors at baseline, 12 weeks and 24 weeks.

Participants for the post-intervention interviews will be identified by investigators based on willingness to be contacted regarding future studies, study adherence and condition assignment to ensure an equal distribution across the latter two variables.

22.2 Source of subjects.

Phase 1. Women will be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study investigator who will provide a description of the study and further screen for eligibility either via on-line screening questionnaires or telephone interview. Eligible breast cancer survivors will be offered the opportunity to participate and will complete informed consent.

If we are not able to sufficiently meet our recruitment goals using the Army of Women©, additional NU resources (e.g. Lynn Sage Breast Cancer Program, RHLCC and the Center for Community Health), on-line forums and social media sites (i.e. Facebook, the Sisters Network and Nueva Vida) and pamphlets fliers at community organizations and events and clinics will be used. Additionally, the PI may send a recruitment e-mail to an existing database of breast cancer survivors. Community representatives will be recruited in conjunction with NU's Center for Community Health (led by Co-I Dr. Ackermann). Experts will be recruited through the RHLCCC and the PI's, co-investigators' professional networks.

Phase 2. Women will primarily be recruited through an e-blast sent to members of the Army of Women©, an online initiative that connects breast cancer researchers with women who are willing to participate in research. The database currently consists of ≥375,000 women and men. Of these, ~30% (112,500) self-report a breast cancer history.

If we are not able to sufficiently meet our recruitment goals using the Army of Women©, additional NU resources (e.g. RHLCC and the Center for Community Health), on-line forums and social media sites (i.e. Facebook, the Sisters Network and Nueva Vida) and fliers at community organizations and events will be used.

Buddies will be identified by study participants.

Participants for the post-intervention interview will be identified by investigators based on willingness to be contacted regarding future studies, study adherence and condition assignment to ensure an equal distribution across the latter two variables.

22.3 Methods used to identify potential subjects.

Phase 1. Breast cancer survivors will be recruited through The Army of Women.© The Army of Women.© will send all women in their database an e-blast to advertise the present study. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study team who will contact them via phone or e-mail to provide a description of the study and further screen for eligibility via on-line screening questionnaires or telephone interview (based on participants preference). Fliers and pamphlets will also be posted in the local community sent to listservs and posted on social media and on-line forums. Additionally, the PI will send a recruitment e-mail to an existing database of breast cancer survivors.

Community representatives will be recruited in conjunction with NU's Center for Community Health (led by Co-I Dr. Ackermann) via personalized e-mails and phone calls. Experts will be recruited through the RHLCCC and the PI's, co-investigators' professional networks via listservs and personalized e-mails and phone calls.

Phase 2. The Army of Women© will send all women in their database an e-blast to advertise the present study. Women interested in participating in the current study will respond to the e-blast. Their contact information will be forwarded to the study team who will contact them via phone or e-mail to provide a description of the study and further

screen for eligibility via on-line screening questionnaires or telephone interview (based on participants preference).

Similar procedures will be followed for survivors recruited through other channels. All interested women will contact study investigators who will provide them with additional details about the study, and if interested, screen them for eligibility.

Buddies will be identified by study participants.

All eligible breast cancer survivors and buddies will be offered the opportunity to participate and will complete informed consent.

22.4 Recruitment materials.

Phase 1. Potential subjects will be recruited using IRB-approved e-blast to the Army of Women©, scripted phone calls and IRB-approved pamphlets/fliers and e-mails.

Phase 2 For survivors, our primary recruitment method will be an e-blast to the Army of Women©. If this is not successful, we will post advertisements on on-line forums and distribute fliers at local community organizations and events. Fliers will be posted and handed out to potential participants.

Potential buddy participants will be identified via breast cancer survivor participants and invited to participate in the online screening by study staff.

Potential post-intervention interview participants will be identified by the study team and invited to participate in the interview by study staff via email.

All recruitment materials will be IRB-approved.

22.5 Payments to subjects.

Phase 1. Survivors will be paid $15.00 via Amazon.com e-gift card following participation in the interview session. Experts and community partners will be paid $20.00 via an Amazon.com e-gift card following participation in each interview session. Survivors will be paid $10.00 via an Amazon.com e-giftcard for each app development session (up to 2) and another $20.00 via an Amazon.com e-giftcard for the field test.

Phase 2. Survivors will be paid $20.00 via check following completion of baseline, 12 week and 24 week follow-up assessments (on-line questionnaires and accelerometer). If they only complete one aspect of the assessment (i.e. wear the accelerometer or answer questionnaires), their pay will be pro-rated to $10 for each component completed. Women who choose to participate in the optional blood sample collection will receive a $15.00 check after receipt of their sample at each of the three time points.

“Buddies” who agree to complete the optional baseline, 12 week and 24 week on-line questionnaire assessments, and complete at least two assessments, will get to keep the Fitbit ($60 value). Those who do not complete at least two assessments will be asked to mail the Fitbit back to the study team.

Participants who agree to participate in post-intervention interviews will be paid $20.00 via Amazon.com e-gift card for participation in this portion of the study.

23.0 Number of Subjects

23.1 Total Number of Subjects to be accrued.

A total of 356 breast cancer survivors, 30 other stakeholders and 128 “buddies” will be accrued.

Phase 1. In phase 1, we plan to recruit breast cancer survivors up to 100 breast cancer survivors, a subgroup (n=30) will participate in interviews and the full sample (n=100) has the potential to participate in the app development sessions and field test. A total of 20-30 experts (n=10-15) (n=10-15) will be recruited for interviews.

Phase 2. For the pilot intervention, we will accrue 256 breast cancer survivors. Approximately 50% of these will be assigned to the buddy condition. As such we will accrue 128 buddies. We anticipate 80% of these “buddies” (n=102) will agree to participate in the optional questionnaire assessments. For the post-intervention interviews, we plan to accrue up to 35 women.

24.0 Provisions to Protect the Privacy Interests of Subjects

24.1 *Steps that to protect subjects’ privacy interests.*

Each participant will be randomly assigned an identification number to ensure confidentiality of data. This will be the only way of matching data with a specific person. Nitro Study Tracker will be the only place where the ID will appear with the participant’s name in the present study. This database will only be accessible by the investigators. This electronic database will house participant contact information and is stored on a secured, password-protected network, accessible only by the investigators.

To ensure the integrity of the data collected from study participants several procedures will be implemented. All personnel involved in data collection will be thoroughly trained in all assessment methods thus ensuring consistent applications of procedures and measurement consistency across participants. All questionnaire assessment data will be automatically saved in the secured, password protected RedCap system and will be downloaded to a password protected network folder protected ensuring access only by the investigators. Any hard copies of data will only include the participants ID number and will be entered into the RedCap system only using this ID number. All raw data will be de-identified (with the exception of the study ID number). These data will be saved to a portable hard drive which will be stored in a locked cabinet in the PI’s laboratory. Any hard copies of data will be stored in a separate, locked cabinet from the informed consents in the PI’s laboratory. Files containing identifying information obtained for purposes of tracking participants and monitoring of subject payments are kept in a locked file in a locked office separate from study related data. Data will only be linked to identifying information through a study ID. Under no circumstances will individually identifiable data be released to anyone without the written consent of the subject. Results will be reported as group findings only. In the past we have found that all of these procedures are effective at reducing risk for study participants.

Issues related to data integrity will be discussed on a weekly basis as a recurring agenda item in the weekly project meeting to ensure constant monitoring of our data integrity. Only the investigators will have access to participant data. All staff with access to the data

with have completed Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules.

Procedures Specific to Phase 1. All interviews and telephone/web-based app development sessions will be digitally recorded whenever possible; digital files will be stored on a password-secured network drive. Only participants' first names will be used during any recorded sessions and participants will have the option of using a "fake" name if they would like. Regardless, all recordings will be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study. Upon download, all data obtained via cellphone, will be de-identified and only be linked to participant via study ID number.

Procedures Specific to Phase 2. RedCap does require an e-mail address to send the survey link to participants. Thus, data will be temporarily linked to individuals' e-mail addresses and first names which may be included in the e-mail for personalization purposes. However, these links will be removed after completion of the questionnaires and these data will then only be linked to the participant's identification number. Upon download, all data obtained via cellphone, will be de-identifed and only be linked to participant via study ID number.

24.1 Steps taken to make subjects feel at ease with research situation.

It will be clearly stated during all phases of this protocol that all subjects will have the option to withdraw at any time for any reason.

Phase 1. All interviews and direct observation app telephone/web-based app development sessions will be digitally recorded; digital files will be stored on a password-secured network drive. Only participants' first names will be used during any recorded sessions and participants will have the option of using a "fake" name if they would like. Regardless, all recordings will be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study. All subjects will have the option to withdraw at any time for any reason.

For the app field study, participants may increase their PA compared to their usual level of PA, although they will be explicitly told this is not the purpose of the field test. Engaging in a PA program when one has been sedentary for a considerable period of time incurs some risk of injury such as l muscle soreness, strains, aggravation of arthritic conditions, etc. However, serious physical injury is considered unlikely. Participants will be instructed to notify study investigators immediately if they experience any adverse effects of using the app.

Phase 2. Engaging in a PA program when one has been sedentary for a considerable period of time incurs some risk of injury such as l muscle soreness, strains, aggravation of arthritic conditions, etc. However, serious physical injury is considered unlikely. In order to reduce and/or prevent any physical harm or injury subjects will gradually increase their PA. Additionally, each participation will be required to pass a screening test or receive medical approval prior to enrollment to ensure PA is appropriate. To make sure subjects are educated on what may be typical, normal side effects of beginning to exercise and what might be more serious, all participants, regardless of the intervention components they receive, will be required to attend an on-line study orientation which

will include an overview of safety issues and stress the need to contact study investigators should they experience any adverse effects of PA. Finally, the intervention content and weekly e-mails will emphasize safety and present instruction to reflect safe progressions.

There are also some potential minimal psychological risks associated with answering some of the questionnaires required for participation in this study. In addition, for those participating in the optional blood sample collection, pricking the finger for the blood sample may cause some minor discomfort. However, we see no psychological, social, or legal risks beyond those of participation in questionnaire based health-related research in general. Regardless, women will have the option to indicate they "prefer not to answer" any questions that make them uncomfortable. Participants will also be instructed that they can withdraw at any time and be provided with the PI's contact information should they have any specific questions or concerns.

All post-intervention interviews sessions will be digitally recorded; digital files will be stored on a password-secured network drive. Only participants' first names will be used during any recorded sessions and participants will have the option of using a "fake" name if they would like. Regardless, all recordings will be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study. All subjects will have the option to withdraw at any time for any reason.

25.0 Compensation for Research-Related Injury

N/A. This study does not involve more than Minimal Risk to the subjects.

26.0 Economic Burden to Subjects

There is no cost to subjects for participation in this study. Should any subject need to park on NU's campus, study staff will cover the cost of parking for the duration of their participants.

27.0 Consent Process

27.1 Consent Process.

Phase 1. All stakeholder participants will complete an on-line version of the informed consent. They will be instructed to print a copy of the informed consent for their records or to contact the study team at any time if they would like a copy for their records.

Phase 2. All breast cancer survivor participants will complete an on-line version of the informed consent. They will also be emailed a copy and instructed to print a copy or to contact the study team at any time if they would like a copy for their records. A telephone number and e-mail address for the PI will be provided on the informed consent page, in the event they should have any questions or need clarification. The informed consent will clearly state that participation in the present study is completely voluntary and participants can discontinue or withdraw at any point without penalty.

All buddy participants will complete an on-line version of the informed consent. They will be instructed to print a copy or to contact the study team at any time if they would like a copy for their records. A telephone number and e-mail address for the PI will be provided

on the informed consent page, in the event they should have any questions or need clarification. The informed consent will clearly state that participation in the present study is completely voluntary and participants can discontinue or withdraw at any point without penalty.

All participants in the post-intervention interviews will complete an on-line version of the informed consent. They will also be instructed to print a copy or to contact the study team at any time if they would like a copy for their records. A telephone number and e-mail address for the PI will be provided on the informed consent page, in the event they should have any questions or need clarification. The informed consent will clearly state that participation in the present study is completely voluntary and participants can discontinue or withdraw at any point without penalty.

27.2 This study is covered by a certificate of confidentiality. This was not included in the original consent form participants signed. All consented participants who are currently enrolled as of 6/14/18 will be informed of this certificate of confidentiality in June 2018 via a letter that will be emailed to the email address we have on file per instructions from the IRB on 6/7/18. ***Waiver or Alteration of Consent Process.***

Initial data collected prior to obtaining informed consent includes name, contact information, and basic medical and health information to determine eligibility for the project. This information is obtained on-line, through a phone conversation or in-person after the subject is given details about the project. These data are recorded in a password protected database only accessible by study investigators. All data are provided freely by the subject. Data for CONSORT purposes will be linked by subject ID, not by name, thus protecting the subject's privacy. Thus, this aspect of the study contains little, if any, risk to the subject. This waiver is requested because determining subject eligibility is only possible by obtaining basic medical healthy history information during screening. Potential participants will be provided with reason(s) for ineligibility via our online tool or initial phone conversation. All subjects will be given the opportunity to be contacted regarding future research opportunities if they so choose, and their contact information will be kept in the database for this purpose. If they prefer no future contact, their name and contact information will be deleted from the database but the information they have previously provided will be used for final CONSORT purposes.

Non-English Speaking Subjects: N/A

Subjects who are not yet adults (infants, children, teenagers): N/A

Cognitively Impaired Adults: N/A

Adults Unable to Consent: N/A

28.0 Process to Document Consent in Writing

Consent will always be obtained before a subject participates in any component of the current protocol. Because we are asking participants to type their full name on any on-line consents, this is considered equivalent to a written signature.

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