Peers Promoting Exercise Adoption and Maintenance among Cancer Survivors

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Objectives / Research Aims

Regular exercise has been recommended by the American College of Sports Medicine for cancer patients and survivors (Schmitz et al., 2010). The recommendations are based on many efficacy trials that have been conducted, chiefly in research settings and delivered/supervised by research staff. Extending the reach of interventions by training community peer volunteers to deliver the intervention makes exercise interventions much more accessible to survivors. Such interventions delivered by community peer volunteers may be relatively inexpensive and may appeal to survivors who would otherwise not seek help. However, such efforts should be effective and have the potential to be easily implemented. Our NIH-funded collaborative research has demonstrated that peer volunteers with the American Cancer Society' (ACS) Reach to Recovery program (a peer-based support program for breast cancer patients) can be trained to deliver a 3-month home-based exercise program to breast cancer patients and the program has been shown to be effective in increasing exercise participation in the short-term (<6 months). But, the effects of the program while continuing to be significant were attenuated at 6 months (compared to the contact control arm). Exercise maintenance is crucial to sustaining the benefits of exercise (fatigue, physical functioning and quality of life) and also to improve survival. Hence, before the program can be implemented in community-based organizations that provide peer mentoring, the maintenance of exercise needs to be addressed. To do so, we propose to develop and test interventions for exercise maintenance (after the 3-month peer counseling for exercise has ended) that can be implemented by a community-based organization, but which vary in mode of delivery (phone vs. email/text), live interaction with the peer mentor (phone), and potentially, cost effectiveness. The specific aims of this randomized controlled trial are:

Primary Aim

1. To determine the effects of Reach to Recovery (RTR) volunteers ("exercise coaches") at American Cancer Society (ACS) offices providing theory-based exercise counseling via telephone over 3 months followed by: a) **exercise logs and feedback reports** during Months 4-9 (Reach Plus), b) **monthly phone calls from coaches, activity logs and feedback reports** during Months 4-9 (Reach Plus Phone) and c) **monthly email/text messages, activity logs and feedback reports** during Months 4-9 (Reach Plus Messages). One hundred and fifty participants will be enrolled in the study. The primary outcome is the change in exercise at 12 months. Our hypothesis is that Reach Plus Phone and Reach Plus Messages participants will report higher moderate-to-vigorous physical activity (MVPA) compared to Reach Plus participants at 9 and 12 months, and that there will be no difference in MVPA in Reach Plus Phone compared to Reach Plus Messages at these time-points. We do not anticipate significant group differences at 3 months.

Secondary Aims

2. To examine the costs related to developing and implementing the interventions (e.g., time spent in training, and supervising the RTR coaches, time involved in intervention development and delivery), costs to the participants and the cost-effectiveness of each intervention. We hypothesize that the Reach Plus Phone and Reach Plus Messages interventions will have higher value compared to the Reach Plus intervention based on quality of life (QOL) and exercise participation.
3. To obtain data on the intervention effects on participants' fatigue, QOL, physical functioning and mood at 3, 9, and 12 months. We hypothesize that Reach Plus Phone and Reach Plus Messages groups will report improvements on these outcomes at 9 and 12 months compared to Reach Plus participants but there will be no significant group differences at 3 months.
4. To examine intervention side-effects (e.g., muscle sprains, injuries) that may occur during

study participation.

Exploratory Aim

5. To examine potential moderators of intervention effects (e.g., age, stage of motivational readiness) and mediators of maintenance of exercise (barriers to exercise, self-efficacy for exercise and social support for exercise) at 9 and 12 months.

A. Research Strategy

A.1. Significance. Improved detection rates and treatments for some forms of cancer have led to significantly improved cancer survival rates over the past half-century. Five-year survival rates for female breast cancer have increased from 63% in the 1960s to 90%.[1] There are over 13.7 million U.S. cancer survivors and, 2.7 million of this group are survivors of breast cancer.[1] Late effects of female breast cancer include poorer physical functioning, arm lymphedema, premature menopause and related infertility and osteoporosis, weight gain, increased cardiovascular risk, fatigue, cognitive impairment, in addition, to risk of cancer recurrence and second primary cancers.[2-4] There is a large body of evidence on the benefits of aerobic exercise participation to alleviate sequelae of cancer treatments when conducted with on-site supervision, as well as home-based programs.[5-9] These data led to the 2010 American College of Sports Medicine guidelines for exercise for cancer survivors.[10] Similar recommendations have been made by the American Cancer Society (ACS).[11]

With the growing evidence of the role that exercise can play in cancer recovery, it is timely to extend the research findings into the "real world" by training community volunteers to encourage survivors to adopt exercise. Our team has been one of the first in disseminating research efforts into the community setting. We chose to test the potential for dissemination in the ACS, a not-for-profit community-based organization (CBO) that offers services to breast cancer patients. Specifically, ACS' Reach to Recovery (RTR) volunteers provide emotional support and information to cancer patients. Hence, it is a "natural fit" to test the effects of volunteers encouraging sedentary survivors to not only become more physically active to enhance their recovery (our randomized trial controlled trial [RCT] described in Preliminary Studies, B.2., showed that the CBO-based intervention was effective, particularly at 3 months), but also to **maintain their activity** to achieve lasting benefits.

A.2. Peer Mentoring for Exercise Promotion. Socio-cultural and communication theories suggest that people are more receptive to assistance when it is delivered by someone perceived as similar to oneself (e.g., of comparable age and life experiences).[12,13] Peer support for health is used to maximize impact, sustain and scale up successful interventions while facing limited resources and contextual constraints. Peer mentoring may be more appealing to patients who would otherwise not seek support. Such evidence-based approaches have been examined in chronic disease management (e.g., HIV, mental illness, and diabetes).[14,15]

There is small but growing evidence on the effects of peer mentors to promote exercise. Quasi-experimental studies support the use of trained peer volunteers providing advice by telephone to middle-aged and older adults.[16,17] In a RCT of 12 volunteer peer mentors and 181 inactive adults aged 50 years and older, researchers compared telephone-based advice delivered by research staff to telephone-based advice delivered by trained volunteers and to an attention control arm of telephone advice for nutrition.[18] Both intervention arms significantly increased their exercise relative to the control group at 12 months, but the peer volunteers showed superior quality in intervention content compared to the research staff. In another RCT, 81 sedentary adults received peer-delivered, theory-based support for exercise in a 16-week group-based program vs. a community-based intervention with health education.[19] At 16 weeks, both groups showed similar significant improvements in moderate-to-vigorous exercise

but at 18 months, the peer support group reported significantly greater exercise participation. These data indicate peer mentoring for exercise promotion is effective but such efforts have not been examined among cancer survivors.

A.3. Theoretical Bases for the 3-month Peer-led Intervention. The telephone counseling component of the proposed exercise intervention will be based on the Transtheoretical Model (TTM)[20,21] and Social Cognitive Theory (SCT) of behavior change that have been applied to exercise behavior. We used this model successfully in home-based exercise interventions among breast cancer survivors,[22] among patients with arterial claudication[23] and among older primary-care patients.[24,25] Reviews and a meta-analysis of the TTM have drawn largely positive conclusions supporting the suitability of the model to understand and promote exercise.[26,27] The TTM model integrates current behavioral status (relating to a performance standard considered healthy) with a person's intention to maintain or change behavior. Five stages of change (motivational readiness) are hypothesized: precontemplation (not thinking about making a change), contemplation (thinking about exercising or other behavior), preparation (engaging in behavior change below recommended levels), action (engaged in behavior change at recommended levels for <6 months) and maintenance (sustained behavior change at recommended levels for $\geq$6 months). TTM-based interventions designed to meet the needs of individuals at each stage are effective in promoting exercise.[28,29] Key constructs from the TTM (motivational readiness) and from SCT (self-efficacy, and beliefs about the importance of exercise in reducing the risk of chronic disease, improve fatigue etc.) underlie the telephone counseling that the exercise coaches will be asked to deliver over 3 months. This will be followed by strategies to enhance exercise maintenance during Months 4-9 using constructs from SCT (self-efficacy) and relapse prevention.[30]

A. 4. Exercise Maintenance. There have been >75 exercise intervention trials for various cancer survivor groups.[9] These trials provided the evidence underlying the ACSM exercise guidelines for cancer survivors.[10] One of the limitations of this body of literature is that while there is a growing support for some of the benefits of exercise adoption, less is known about the maintenance of exercise and the implications for the benefits (improved fitness, higher quality of life [QOL], reduced fatigue, etc.). Exercise maintenance is critical to the management of cardiovascular disease, diabetes and other chronic diseases among cancer survivors as well as potentially for cancer survival.[31-34] We have found that the psychosocial benefits of exercise for cancer patients did not sustain if the behavior is not maintained for at least 6 months.[35] Maintenance of outcomes is also fundamental to inform the translation of evidence-based behavior interventions into practice.[36]

Maintenance has been defined as a follow up evaluation of a behavioral outcome occurring at least 3 months postintervention contact.[37] A review of 29 trials that targeted either exercise alone, diet only or both exercise and diet found that 72% of the studies achieved maintenance of behavior change.[37] The authors reported that maintenance was associated with sample characteristics (studies targeting women were less likely to achieve maintenance), study method (trials with higher retention showed higher maintenance) and intervention features such as *intervention duration* (>6 months), face-to-face contact, use of more intervention strategies and the use of follow-up prompts. A recent review of exercise and/or dietary interventions in breast cancer survivors, found that only 10 trials assessed post-intervention maintenance of outcomes, and only four trials achieved successful maintenance of behavior change for at least 50% of outcomes.[38] This review suggested that extending program contact with participants may promote maintenance but no conclusions could be reached as to the most effective maintenance strategy. To date, there is limited evidence to suggest which strategies support exercise maintenance in chronically ill[39] and healthy populations[40] and whether these differ from those known to support exercise initiation.

Given our partnership with the RTR program within the ACS, we have selected to compare maintenance strategies (behavioral component of self-monitoring, follow-up email/text messages to remind and motivate, and continued contact with the peer volunteers) that are based on the literature and are likely to be feasible for implementation by CBOs. We considered the use of other technologies such as smartphones but chose email/text for one intervention group because the latter is simple, widely used by the ACS, likely to have a wide reach, and can be disseminated in not-for-profit CBOs. The total intervention duration will be for 9 months (Months 1-3: Exercise Adoption, Months 4-9: Exercise Maintenance). We will also explore potential moderators of exercise maintenance (age, motivational readiness, stage of disease) to address questions such as who benefits from which maintenance strategy and mediators of intervention effects (e.g., self-efficacy).

A. 5. Reach to Recovery (RTR) Program. For over 35 years, the RTR program has helped people cope with breast cancer. RTR volunteers, who are breast cancer survivors themselves, give support for those with a new diagnosis, breast cancer recurrence or metastasis. The volunteers offer understanding, support and hope because they themselves have survived breast cancer and have gone on to live productive lives. Volunteers are carefully selected, complete initial training, and participate in ongoing continuing education sessions. There are >13,000 volunteers with the RTR program: it is now the largest peer one-on-one program offered by the ACS. Hence, if the results of this RCT are promising, the intervention for exercise adoption and maintenance can be integrated into the current services offered by the RTR program and tested in ACS offices (or other cancer care CBOs that offer peer support) in other states in a larger, dissemination trial.

B. Preliminary Studies

Dr. Pinto (Principal Investigator, P.I.) has developed programmatic research on exercise promotion to enhance recovery among cancer survivors over the past 20 years. She has developed and demonstrated the efficacy of home-based exercise programs among breast[22,41,42] and colorectal cancer survivors.[43] The following studies have been selected to document the team's ability to conduct the trial and to describe the groundwork for the scientific and practical viability of the proposed study.

B.1. Exercise Intervention Delivered by American Cancer Society's Reach to Recovery Volunteers. We recruited Reach to Recovery (RTR) volunteers with the American Cancer Society to offer our effective telephone-delivered home-based exercise program[22] to 25 breast cancer survivors (study funded by the Lance Armstrong Foundation).[42] The program based on the TTM of Behavior Change and Social Cognitive Theory was offered over 3 months and outcomes were assessed at 3 and 6 months. Seven RTR volunteers were recruited as exercise coaches (mean age = 59.6 years; mean number of years volunteering with RTR = 7 years). Coaches received 10-12 hours of training and were asked to contact their participants weekly for 3 months (12 weeks=12 calls) and audio-tape their telephone contacts. The research team reviewed the audio-tapes and provided bi-weekly supervision of the coaches via phone. Research staff conducted the participants' assessments at baseline, 3 and 6 months. Results: Using t- tests to examine changes from baseline, we found that participants significantly increased moderate-to-vigorous physical activity (MVPA as assessed by the 7 Day Physical Activity Recall) from baseline to 3 months ($p<.0001$) and from baseline to 6 months ($p<.01$). Effect sizes were large (Δ=0.99 at 3 months) to moderate (Δ= 0.62 at 6 months). For the psycho-social outcomes, significant reductions in the effects of fatigue were reported both at 3 months ($p<.0001$) and 6 months ($p<.001$) compared to baseline. The effect sizes were large at both time-points (Δ=0.78 and Δ=0.89 respectively). Mood (assessed by the Profile of Mood

Scale, Total Mood Disturbance score) did not show changes at 3 months but there were significant improvements at 6 months ($p<.01$) (effect size was moderate, $\Delta=0.69$). Feasibility and Acceptability of the Intervention. Coaches' perspective: RTR coaches were able to deliver 93% of expected calls; the mean number of calls across participants was 10.72 (maximum number of calls was 12; SD=2.5) with a mean duration of 15.22 minutes (SD=6.11). All the coaches recommended the program to future participants. Participant evaluations: At 3 months, participants (n=22) also rated the program very favorably with a mean rating=4.8, SD=0.5 (1-5 rating scales, 1=Low, 5=High). 91% judged the weekly calls to be the appropriate length and 96% judged the number of calls to be about right. 91% reported that they would recommend the program to others. In sum, we obtained preliminary data on the intervention effects, tracked side-effects of study participation and obtained feedback from the participants. In addition, we refined the training materials and procedures to make them appropriate and feasible for coaches, refined our supervision of intervention delivery, and obtained data on the feasibility of volunteers' offering the intervention.[42]

B.2. Randomized Trial of Exercise Counseling Delivered by American Cancer Society's Reach to Recovery Volunteers. Based on our pilot work (Preliminary Studies, B.1), in an on-going study (R01 CA132854), we trained 18 RTR volunteers in six states to deliver the 3-month exercise counseling to 76 breast cancer patients (B. Pinto, P.I, K. Stein, S. Dunsiger, Co-Is). We compared the effects of exercise counseling delivered by telephone by RTR coaches (Reach Plus) vs. a contact control condition (Reach Standard) in 6 New England states. The coaches (n=18; mean age=54.9 years, mean years with the RTR program=4.2) delivered the 3-month exercise program to help participants adopt 30 minutes of MVPA on $\geq$5 days/week. Breast cancer survivors (n=76; mean age=55.6 years, mean years since diagnosis=1.1 years) were randomized to Reach Plus or Reach Standard. At pretreatment, posttreatment (3 months) and 6 months, participants completed the 7 Day Physical Activity Recall, wore an accelerometer and completed measures of fatigue (FACT-F) and QOL (FACT-B). Mixed effect longitudinal regression models for between group differences at 3 and 6 months, while controlling for age and chemotherapy showed significant effects for MVPA in Reach Plus at 3 months (adjusted mean difference = 102.95 minutes/week of MVPA, $t=6.6, p<.0001$) and at 6 months (adjusted mean difference = 34.7 minutes/week of MVPA, $t = 2.23$, $p=.02$). Effects on self-reported exercise were confirmed with similar analyses on accelerometer data on MVPA at 3 months (adjusted treatment difference of 48.5 minutes/week, $t = 4.08$, $p<.0001$) and at 6 months (treatment difference of 38.7 minutes/week, $t = 3.22$, $p<.01$).[44] Data analyses of secondary outcomes are on-going. There were no serious adverse events related to exercise. Coaches delivered 92.98% of expected calls; mean number of calls across participants was 11.16 (max. number of calls was 12; SD=2.24) with a mean duration of 18.46 minutes (SD=7.36). All the coaches recommended the program to future participants (100%). This study demonstrates our ability to train peer volunteers (exercise coaches) in several states to provide exercise counseling using both in-person training and videoconferencing, supervise exercise coaches, collect data from patients who received the exercise counseling and assess effects of the exercise counseling on patients' exercise participation, the primary outcome in the proposed work. However, while it is clear that the intervention when offered by peer coaches facilitated exercise adoption, the effects on exercise maintenance (6 months) were not as strong. Hence, in the current proposal, we will implement and test strategies for exercise maintenance before dissemination to RTR programs in other states or other cancer care organizations. Our goals are to obtain data that peer volunteers can help breast cancer survivors adopt and maintain exercise by testing the effects of evidence-based maintenance strategies in a community setting.

C. Setting
As described, the coaches who participate in the study will be recruited chiefly by the American Cancer Society through mailing lists that they maintain. Training of coaches will be done via video-conferencing or at ACS offices. Study assessments will be conducted with the coaches via mailed questionnaires and telephone. Study participants will be recruited with the help of the American Cancer Society, Palmetto Health, South Carolina Oncology Associates. All study assessments will be done via mail and the exercise interventions will be delivered by telephone and by mail.

D. Study Design
This is a randomized controlled trial where 150 breast cancer survivors will be randomized to one of 3 intervention groups: Reach Plus, Reach Plus Phone and Reach Plus Message. Participants will complete assessments of MVPA and psychosocial variables at baseline, 3, 6, 9 and 12 months. The unit of randomization will be at the patient level. Intervention delivery will end in Month 9.

D.1. Recruitment Methods
ACS RTR Volunteers. An orientation to the study and procedures will be conducted at each collaborating ACS office as we have done previously (Preliminary Studies, B.2). Currently there are 1690 RTR active volunteers in the South Atlantic Division, and there are 765 RTR volunteers at the ACS offices in GA and NC that will collaborate on this trial. We will recruit 10-12 volunteers from this group to be trained as "coaches." Each coach is expected to work with 15-18 participants over the study duration. Dr. Kevin Stein (Managing Director of Behavioral Research at the ACS National Office that oversees the RTR programs) and Ms. Shanna Lee (Director, Mission Delivery, South Atlantic Division) have provided us letters of collaboration; they will assist us in recruiting volunteers to serve as coaches and to identify breast cancer patients on ACS constituent mailing lists who may be eligible for study participation. As in our prior work (Preliminary Studies, B.1. and B2), we will mail informational letters to RTR volunteers offering them the opportunity to be "coaches." These letters will include testimonials from the coaches in our prior collaborations. Rolling enrollment and training will be offered.

Due to the changes within the American Cancer Society's organizational structure and the RTR program, there is a need to recruit additional coaches using alternative methods. Volunteers who are breast cancer survivors will be invited to be trained as coaches. RTR training will be provided to volunteers as part of the study's training plan. The American Cancer Society has agreed to allow interested volunteers to be trained using their online training RTR modules. We will send an informational flyer to previous study participants and others who have expressed interest in participating in the study but were too active to do so. Upon completion of the RTR training, all training methods for interested coaches will proceed as we have done previously.

Patient Population/Participant Recruitment. ACS offices will be asked to send informational mailings to their breast cancer constituents lists in GA and NC (current listing, n=6980). In addition, if necessary, we can recruit from mailings sent to breast cancer constituents in MD (n=1467). The South Atlantic Division has 14,183 cancer survivors within 5 years of diagnosis on their mailing lists. We will also recruit from private oncology practices in SC (e.g., South Carolina Oncology Associates that have provided referrals to cancer survivorship studies conducted by the College of Nursing). Patients will be provided brief information about the study and will be asked if they wish to participate. Interested participants will be asked to view an introduction to the study video and complete online pre-screening questions on the study's webpage prior to contacting the study team. The study's participant recruitment brochure and cover letter will be revised to include instructions for accessing the video and pre-screener

questions. Those who are preliminarily eligible will be contacted by study staff to complete the full telephone screen for eligibility. The study's Project Coordinator I will explain the study to them and obtain verbal informed consent to conduct a telephone screen for eligibility. If eligible on the phone screen, the Project Coordinator I will send the participant an informed consent document in the mail, along with a physician consent form for the patient's participation in the study. The informed consent will also be offered electronically via a link being sent to the participant for review and completion. The research staff will receive a notification when the informed consent has been completed. Research staff will re-contact potential participants in two weeks, if the signed consents are not received, to prompt and respond to any questions that may arise. After the consent forms are obtained, participants will be mailed a packet of questionnaires and an Actigraph (an accelerometer to monitor exercise) with instructions and envelopes for returning the questionnaires and Actigraph. In addition to mail, the baseline assessment will also be offered electronically via a link being sent to the participant for completion. The research staff will receive a notification when the baseline assessment has been completed. After the completed forms and Actigraph are received, the Project Coordinator I will contact the participant to conduct a physical activity interview (7 Day PAR, described in Outcomes section). After the baseline assessments are completed, the participant will be randomized to one of the three study groups.

Records show that approximately 8447 breast cancer patients (<5 years post-diagnosis) on the ACS mailing lists for GA,NC and MD (ACS South Atlantic Division, 2014). Our target population is breast cancer survivors who are not already exercising. In our previous trial where we used similar inclusion/exclusion criteria (Preliminary Studies, B.2),13% of those screened were eligible and enrolled in the study (a major reason for ineligibility was women reported already exercising and for non-participation, the major reason was unwillingness to be assigned to the control group which did not receive an exercise intervention). Using these data, we estimate that 2365 patients will be screened for eligibility and 307 (13%) of those screened will be eligible and enroll in the study. If necessary, we can also extend participant recruitment to the remaining South Atlantic states (SC, VA, WV, and DE), where there are 5736 breast cancer patients on the ACS mailing lists. Using the same estimates, 1696 patients will be screened, 209 patients should be eligible and enroll in the study (total number of eligible patients who will enroll= 307+209=516). In the proposed study, all study groups will receive an exercise intervention, and we expect that this will enhance recruitment and generalizability of results to the population of survivors who do not exercise. Hence, we fully anticipate enrolling 150 women over 2 1/2 years from the sample of 516 eligible patients who would be willing to participate in the study.

D.2. Sample Randomization. Each participant will be asked to obtain medical consent from her oncologist to enroll as we have done successfully in prior work (Preliminary Studies B.1-B2). Providers will be allowed to exclude patients if the goal of moderate-intensity exercise would be unsafe for the patient. Randomization will occur after informed consent and baseline data are obtained. The sample will be stratified for two variables that may affect exercise outcomes (age:<60 years/≥60 years; and treatment: received/not received chemotherapy). After baseline assessments, the Project Coordinator II will contact the participant and disclose group assignment from a code number found in a sealed envelope. We will use block randomization with varying block size at each collaborating ACS office, so that equal numbers of participants are randomized to Reach Plus, Reach Plus Phone and Reach Plus Messages at each site. After a participant has been randomized, the Project Coordinator II will determine coach assignment based on similarity of age, type of cancer treatment and availability for calls at the times preferred by the participant. Each coach will be instructed to call her participant once a week over 3 months (12 weeks=12 calls) at a mutually convenient time.

Participants will receive $25 for completing the assessments at each time-point ($25 X 5=$125). In addition, they can receive $25 for completing 80% of exercise logs.
Coaches will be provided small incentives such as $25 gift cards at various points in the study (e.g., after working with their first study participant, at the end of the year).

D.3. Inclusion and Exclusion Criteria
Eligibility Criteria for RTR coaches includes: 1) completed RTR training and has been with RTR for at least a year, 2) willing to participate in group training scheduled at a mutually convenient time, 3) willing to audio-tape contacts with participants for quality control, 4) willing to be supervised via phone and 5) currently exercise for at least 60 minutes/week. Coaches will be asked to complete brief questionnaires before training, at the end of training and at the end of study participation.

Eligibility Criteria for Participants. Women aged ≥21 years will be eligible if they: 1) have been diagnosed in the past five years with Stage 0-3 breast cancer (patients on radiation or chemotherapy will be eligible as will patients receiving hormone therapy: physician consent for all study participants will be obtained), 2) are able to read and speak English, 3) are ambulatory, 4) are sedentary (i.e., <30 minutes/week of vigorous exercise or <90 minutes/week of moderate-intensity exercise for the past six months), 5) are able to walk unassisted, and 6) have access to a telephone. Women with more advanced disease (Stage 4), medical or psychiatric problems (e.g., substance abuse, coronary artery disease, peripheral vascular disease, diabetes, and orthopedic problems) that may interfere with protocol adherence will not be included. These inclusion/exclusion criteria are similar to those used in our prior work (Preliminary Studies, B.1. and B.2). Participants will be asked to provide consent for medical chart review to extract disease and treatment history.

D.4.Study Endpoints
Primary Endpoint
The primary outcome is the change in exercise at 12 months. Our hypothesis is that Reach Plus Phone and Reach Plus Messages participants will report higher moderate-to-vigorous physical activity (MVPA) compared to Reach Plus participants at 9 and 12 months, and that there will be no difference in MVPA in Reach Plus Phone compared to Reach Plus Messages at these time-points. We do not anticipate significant group differences at 3 months.

Secondary Endpoints
Costs related to developing and implementing the interventions (e.g., time spent in training, and supervising the RTR coaches, time involved in intervention development and delivery), costs to the participants and the cost-effectiveness of each intervention.

Intervention effects on participants' fatigue, QOL, physical functioning and mood at 3, 9, and 12 months. We hypothesize that Reach Plus Phone and Reach Plus Messages groups will report improvements in these outcomes at 9 and 12 months compared to Reach Plus participants but there will be no significant group differences at 3 months.

D.5. Procedures
Intervention Conditions. All three study groups will be structurally equivalent with respect to the 3-month exercise intervention (12-weekly calls from RTR coaches, exercise logs, pedometer and feedback reports).

Reach Plus. In Months 1-3, participants in this group will be receive the previously tested telephone counseling for exercise[22] (Preliminary Studies, B.1., B2) that consists of exercise

counseling matched to participants' motivational readiness, exercise logs, a pedometer (Digiwalker) and feedback reports. These components are: a) Exercise Counseling: RTR coaches will be asked to contact participants by telephone weekly over 3 months (12 calls). Each call will take about 10-15 minutes. The purpose of these contacts is to build a supportive relationship with the participant, assess motivational readiness, monitor exercise participation, identify any health concerns, assist the participant to identify relevant barriers to exercise and help her to problem solve to overcome such barriers. In addition, the coach will provide feedback, reinforce and encourage efforts to start or stay active. The counseling will be matched to the patient's motivational readiness assessed at the start of each call. Women in the precontemplation stage will be given messages to increase their awareness of the benefits of exercise after cancer treatments (e.g., improved physical functioning). Those in the preparation stage will receive specific information on how to increase exercise in a safe and appropriate manner (e.g., to reduce risk of lymphedema).

The goal for the 3-month program, as in prior work, will be to gradually increase the amount of moderate-intensity aerobic exercise that is performed, for example, increased walking, yard work, and sport if appropriate, to the current recommendations of at least 150 minutes of MVPA per week.[10,45] Previous studies have shown that walking is the preferred form of exercise among U.S. adults and cancer survivors.[46] If participants have access to home exercise equipment, they will be free to participate in moderate-intensity exercise of their choice. Our goal is to promote aerobic exercise that is feasible and enjoyable for participants.

Motivational readiness for exercise (assessed at each call) is a key construct of the intervention. As in our prior work (Preliminary Studies, B.1. and B.2), the coaches will be trained to tailor the exercise counseling to the participant's stage of readiness. The strategies for working with participants in Precontemplation stage of readiness are different from patients in Preparation. For example, action-oriented messages (e.g., "it is important for you to remind yourself to exercise") would not appropriate to someone who is not intending to start becoming active. The supervision of exercise coaches will include attention to tailoring to motivational readiness. Similarly, the audio-taped calls will be audited for attention to motivational readiness both as a content component and a process element.

A key element in RTR coaches offering the intervention is that they are peers who have also survived breast cancer. In this sense, they can relate to the patient from a different perspective than research staff. Participants and coaches can share their experiences with cancer diagnosis, treatment and recovery. However, the coaches will be told NOT to provide medical advice and will be trained to encourage participants to contact their oncologist/primary care physician for medical care/health issues. If participants report symptoms such as chest pain or difficulty breathing, participation will be temporarily suspended and they will be referred to their oncologist (See section on coach training).

b) Exercise Logs: As in our prior work, participants will be asked to monitor frequency, duration, and intensity of exercise and any side-effects on exercise logs during the 3-month program. Heart rate monitors and pedometers will be provided and readings will be recorded on exercise logs as we have done previously.[41,42] The coach will review the weekly logs during calls and help to problem solve barriers to exercise. We will use incentives to encourage maintaining logs.[22,25] c) Pedometer: Participants will be encouraged to use a pedometer (Digiwalker) during aerobic exercise such as walking and record steps on the exercise logs. d) Feedback reports: Participants will receive these reports at 2, 4, 8 and 12 weeks (Preliminary Studies, B.2) that summarize their progress, barriers they identified during the calls and ways to overcome the barriers as discussed during the calls.

Maintenance Program (Months 4-9). Unlike our previous RCT, after the 3 months are

completed, participants will be provided exercise logs for the remaining months. They will be encouraged to use the heart rate monitors and pedometers during exercise. They will be asked to mail/e-mail the logs to study staff each month and a monthly feedback report showing their progress and encouraging exercise maintenance will be sent to them. Participants can choose mail or email as their preferred mode. Incentives ($25) will be provided for those who return at least 80% of the logs. Self-monitoring is an evidence-based technique for behavior change[47] and we expect that providing feedback reports will be a less costly approach that CBOs can implement to support exercise over the long-term.

Reach Plus Phone. As noted earlier, participants in this group will receive the same 3-month exercise counseling intervention described above for Reach Plus. However, after the 3-month assessments have been completed, the coaches will be asked to continue to contact their participant each month during Months 4-9 (one call per month, a total of 6 additional calls). These calls are expected to take about 10 minutes. We chose to extend and taper the calls from the coaches because: a) Participants in our prior trial (Preliminary Studies, B.2.) rated the telephone calls from the coaches as the most helpful program component (mean of 4.97, scale 1-5, 1=not at all helpful, 5=very helpful) and so we have retained this highly rated intervention contact, b) Among those who made recommendations to improve the intervention (n=17), 58% expressed a preference for a longer contact with the coach, and c) The literature on PA interventions shows that those of longer duration (>6 months) had better maintenance, so we have extended and tapered the contact beyond 3 months to Month 9.[37] We will focus the calls on principles from Social Cognitive Theory[48] and Relapse Prevention Theory[30] and the participant's stage of motivational readiness. As in Months 1-3, all calls will begin with an assessment of exercise and motivational readiness so that the calls are tailored to motivational readiness. In addition, the calls will target self-management approaches including cognitive (goal setting, identifying barriers and problem solving), behavioral (self-monitoring using exercise logs and the pedometer) and environmental strategies (developing social support) that have been recommended for exercise maintenance.[49] The call content will include a brief review of monthly exercise logs, problem solving and negotiation of exercise goals for the next month. Specific attention will be made to prevent lapses to sedentary behavior by anticipating and preparing for lapses, developing a plan to recover from lapses and return to regular exercise and developing and using social support for sustaining exercise. Participants will be asked to monitor their exercise using logs (they will be encouraged to use the heart rate monitors and pedometers) for which they will receive an incentive ($25), mail/email the exercise logs back to the research staff and a monthly feedback report will be mailed/e-mailed to the participant (participants can choose preferred delivery mode). Our experience and those of other researchers[50] show that exercise maintenance can be enhanced by using periodic phone contact to address patients' concerns and to review exercise logs. Hence, these participants will have the opportunity to continue to receive support from their coach during brief calls in Months 4-9.

Reach Plus Messages. As noted earlier, participants in this group will receive the same 3-month exercise counseling intervention described above for Reach Plus. However, after their 3-month assessments have been completed, participants will receive brief messages by email or text (participants can choose their preferred mode of contact) to motivate, prompt and reinforce continued exercise. The rationale for this approach is based on: a) the literature where prompts/reminders have been found to be effective to sustain behavior change [38,51] and b) feedback from the ACS on maintenance techniques that are feasible for the organization (per consultation with Dr. Kevin Stein, National ACS). Although ACS uses various communication methods to reach constituents, email is the "go-to" channel for most of their communications (personal communication, Ms. Hilary Noon, Vice President Custom Experience, Insight & Analytics). These messages will be sent by the research staff in collaboration with the RTR ACS

executive and will be personalized using both the name of the participant and name of her coach. An example: “Hello (participant’s name), your coach, Ann, and the RTR program would like to remind you that staying physically active will provide you both mental and physical health benefits. We encourage you to exercise for at least 150 minutes each week.” The messages are intended to support motivation for exercise, remind participants of the benefits of exercise for cancer survivors and provide encouragement to stay active. The messages will be tailored to the stage of readiness and exercise reported on the previous assessment (i.e., message in Month 5 tailored to readiness for exercise reported in Month 4). We will develop a standardized message specific to each stage of readiness: for example, women in Preparation will hear the same message but individualized using the name of the specific coach. We will develop a library of 24 messages for each stage of readiness over the 6-month maintenance phase. There will not be an opportunity for the coach to counsel the participant during Months 4-9 and for the participant to interact with the ACS as a contrast to Reach Plus Phone. The messages are purposefully meant to be a brief, potentially low-cost, feasible approach that the ACS can implement to help survivors stay physically active. There will be a total of 24 messages during Months 4-9 (one message/each week). Participants will be expected to monitor their exercise using exercise logs (they will be encouraged to use the heart rate monitors and pedometers) for which they will receive an incentive ($25), mail or email the exercise logs back to the staff on a monthly basis and a feedback report will be mailed (or e-mailed) to the participants (Months 4-9).

D.6. Training Exercise Coaches. Dr. Pinto will train the coaches in-person at the collaborating ACS offices or via videoconferencing. Based on our prior trial (Preliminary Studies, B.2), we anticipate that 4 sessions each lasting about 2 1/2 hours will be needed for training. Session 1 will consist of didactics on benefits of exercise for cancer survivors, and a review of the manual. Sessions 2-3 will focus on skills and counseling techniques (e.g., empathy, reflective listening), didactics on the use of the TTM Model and social cognitive theory to promote exercise adoption and maintenance, working with human subjects and HIPAA regulations, as well as emergency protocols if participants report potentially dangerous health symptoms during or after exercise (e.g., chest pain) or report emotional distress. Coaches will be trained to query participants at each call about a list of symptoms and notify research staff immediately if participants endorsed any symptoms that the trainers noted were potentially indicative of a serious problem. In these cases, study participation will be temporarily suspended until the medical issue has been resolved. If participants become distressed, appropriate referrals will be made. Training methods will include listening to audiotapes of exercise counseling and practice role-plays with trainer feedback. For the proposed study, we will also add training to focus on exercise maintenance in Session 4 (for the Reach Plus Phone group), with additional role plays on lapse prevention and lapse recovery for exercise maintenance. To determine proficiency, we will train coaches to demonstrate key skills with 3 standardized participants; training will end when coaches can cover at least 80% of the content areas, and demonstrate a score of $\geq$4 on each of 8 process indicators (1-5 rating scales). Additional training will be offered until criteria are met. All training materials are already available.

D.7.Quality Control. All telephone contacts with participants will be audio taped. The Project Coordinator II will review a random sample of 50% of the contacts weekly to monitor safety and fidelity to protocol. Dr. Pinto will audit a random sub-sample (10%) of the calls in each group for quality control. The Project Coordinator II will provide feedback and supervise the coaches during bi-weekly telephone supervision. Corrective feedback will be provided. Booster training will be provided periodically in Years 02-04. Quality control procedures will help ensure that coaches adhere to the protocol for each arm to minimize potential contamination across conditions and/or differences in enthusiasm for one condition vs. the other.

D.8. System Support for Coaches. The coaches in our prior work (Preliminary Studies, B.1. and B.2.) were very satisfied with study participation. Based on their feedback, factors such as the convenient access to the training location, food at the training sessions, and telephone supervision (rather than in-person supervision) during intervention delivery were cited as important to their volunteer roles in this research collaboration. Hence, we plan to offer food at training sessions, small incentives to the coaches (e.g., $25 gift certificates) and supervision via telephone to support their roles. We will provide them audio-taping equipment.

D.9. Measures to Ensure Internal Validity. The following steps will be taken to assess possible threats to internal validity and/or alternative explanations of significant effects or failure to find effects:1) Treatment Validity: Protocols will be used for the phone calls in all groups for the first 3 months as well as the monthly phone calls for the Reach Plus Phone group during Months 4-9. To ensure fidelity in the interventions, we will ask coaches to audio tape their calls to participants. Review and auditing of calls has been described previously. We will provide re-training if drifts from study protocol are noted. Participants will be asked to evaluate the benefits of the calls and the general social support of the phone contact.

2) All participants will be asked at 3, 6, 9 and 12 months if they have received counseling and/or sought other treatments that may attenuate fatigue and other outcomes. Participation in other exercise or psychosocial programs will confound our results and hence, we will collect data on such participation, and use it as a co-variate in the outcome analyses.

E. Outcome Measures. Similar to our prior work (R01 CA 132854),assessments at 3, 6, 9 and 12 months will follow the same procedures as for the baseline assessments: the questionnaires and accelerometers will be mailed to participants. When the completed questionnaires and the units are returned by mail, the Project Coordinator I ("blind" to the participant's group assignment) will call the participant and conduct the 7 Day PAR interview by phone. Participants will receive $25 for completing the assessments at each time-point ($25 X 5=$125). Note: At 6 months, women will complete only a partial selection of exercise and measures of psychosocial constructs *to* conduct mediational analyses, increase power and for comparison with our prior trial (R01 CA 132854). The full battery of assessments includes:

Table 1: Assessment Schedule for Participants

	Baseline	3M	6M	9M	12M
Patient demographics	x				
Medical chart information	x				
7 Day PAR	x	x	x	x	x
Actigraph	x	x	x	x	x
Fact-F (Fatigue)	x	x		x	x
FACT-B (QOL)	x	x		x	x
Profile of Mood States	x	x		x	x
SF-36 Health Survey	x	x		x	x
Motivational Readiness	x	x	x	x	x
Social Support for Exercise	x	x	x	x	x
Self-Efficacy for Exercise	x	x	x	x	x
Physical Activity Enjoyment	x	x	x	x	x
Exercise Barriers	x	x	x	x	x
Intervention evaluation		x			x

E.1.Primary Outcome (Aim #1)

1. Seven Day Physical Activity Recall (7 Day PAR).[52] This interviewer-administered measure,[53] is widely used and validated measure of occupational and leisure activity. It assesses hours spent in sleep, moderate activity, hard and very hard activity. Caloric expenditures are estimated based on the metabolic equivalents for the different activity classes. We will obtain the total minutes of MVPA as our key outcome measure, similar to other national trials of exercise programs.[54] We will administer the 7 Day PAR by telephone at each time-point.

2. Accelerometer: As in the prior RCT, we will use the Actigraph accelerometer (GT3X) as an objective measure of exercise. Participants will be asked to wear the Actigraph for 7 days at each assessment point (concurrent with the seven days of the 7 Day PAR interview). Based on our prior work and the work of other researchers,[55,56] we expect that any reactivity to wearing the units will be similar in the study groups at baseline, and that reactivity will decrease in all groups over time.
The following questionnaires will be mailed to participants at each assessment and returned by mail. The Project Coordinator I will review completed questionnaires and re-contact participants to minimize missing data.

E. 2. Secondary Outcomes (Aim #3). QOL, physical functioning, fatigue and mood will be assessed using standardized questionnaires: Functional Assessment of Cancer Therapy Scale-Breast (FACT-B),[57] 36-item Short Form Health Survey that includes a Physical Functioning subscale,[58] Functional Assessment of Cancer Therapy Scale-Fatigue (FACT-F),[59] and the Profile of Mood States.[60]

Questionnaires will be used to assess **constructs relevant to the TTM and SCT**: Stage of Readiness for Exercise[61] and Exercise Self-Efficacy[62] that are designed for telephone or mail administration. Motivational readiness and self-efficacy will be examined as a potential moderator and mediator (respectively) of intervention effects.

E.3. Potential Mediators. (a) Social Support. We will use the Social Support for Exercise Survey, a reliable scale that assesses support from friends and from family members[63] to assess the meditational role of this construct. (b) Physical Activity Enjoyment. This construct will be assessed using the 18-item Physical Activity Enjoyment Scale.[64] Participants will be asked to rate "how you feel at the moment about the physical activity you have been doing," using a 7-point bipolar rating scale. Enjoyment has been found to predict exercise maintenance.[49] (c) Exercise Barriers. This 21-item measure assesses how often situational barriers prevented participants from being active in the previous 3 months and a composite barriers score will be determined[49]. (d) Exercise Coach. Coaches will be included as a random effect.

E.4. Exercise Adherence. Participants will be asked to maintain exercise logs (i.e., the frequency, duration and type of exercise, heart rate during exercise, pedometer steps and any health problems). Coaches will review the logs during weekly calls in Months 1-3 (Preliminary Studies B.1-B.2). Similar logs will be used by all participants during Months 4-9 and sent to research staff. Incentives will be provided for maintaining the logs.

E.5. Adverse Effects of the Interventions (Aim #4). As in previous studies, during telephone calls (Months 1-3), the coach will review the exercise logs and ask questions about any problems related to exercise to track adverse events. During Months 4-9, participants will be asked to report any adverse events (e.g., sprains, chest pain) to the study staff when they occur and record these events on the exercise logs.

E.6. Evaluation of the Interventions. a) Coach Evaluations. At the end of their study participation, all coaches will complete an evaluation of the training and supervision. The perceived acceptability and usefulness of the interventions will be assessed using a questionnaire (Preliminary Studies, B.1 and B.2). b) Participant Evaluations. At 3 months and at 12 months, all participants will evaluate the intervention they received and its components (e.g., usefulness of calls, email messages) as we have done in prior trials.[22,65]

E.7.Fidelity of Interventions. In addition to quality control procedures, we will record the number and the duration of calls delivered to all study participants in Months 1-3. Such tracking will continue during Months 4-9 in the Reach Plus Phone group. We will track exercise logs received during Months 4-9 and feedback reports sent to all participants. We will track the number of email/text messages sent to the Reach Plus Messages group in Months 4-9. These data will be indicators of fidelity in intervention implementation.

E.8. Background Variables. These variables are the participant and coach characteristics that may affect MVPA, our primary outcome. Participant Characteristics. (1) Baseline demographic Information (age, marital status, ethnic group, education, etc.) will be assessed using standard questions from national surveys. (2) Disease and treatment variables: The participant's disease and treatment history (date of cancer diagnosis, cancer stage, treatments received) will be extracted from medical records after obtaining permission during informed consent procedures. If women refuse to give permission, they will not be eligible for the study.

E.9. Coach Characteristics. Prior to training, coach characteristics such as age, time with RTR as a volunteer, time since diagnosis of breast cancer and experience with exercise counseling will be assessed with a brief questionnaire. We will also assess their knowledge and beliefs about exercise counseling using a questionnaire (Preliminary Studies B.1-2). At posttraining, a brief assessment of knowledge about exercise counseling, confidence in providing counseling and an evaluation of the training will be conducted. At study end, coaches will be asked to evaluate the interventions they delivered.

Table 2: Assessment Schedule for RTR Coaches

	Study Start	Post-training	Study end
Demographics Knowledge of exercise, and beliefs about exercise	X X		
Knowledge test Confidence in exercise counseling Training evaluation		X X X	
Final evaluation (study and intervention)			X

E.10. Cost Effectiveness (Aim 2). Cost-effectiveness analysis is a method for assessing the relative value of health programs.[45,66] We will collect data on costs of delivering each intervention to better understand the potential for disseminating the intervention(s). To date, very few studies that offered an exercise intervention for cancer survivors has provided data on costs.[8] Data collection and analysis will follow guidelines of the Public Health Service Panel on Cost-Effectiveness[67] and other well-established recommendations.[68] Intervention costs will include costs of training the coaches, the marginal costs of personnel, printing, postage, telephone and facility costs. Personnel costs will be calculated from intervention delivery by the coaches, time logs maintained by the Project Coordinator II (who will supervise the coaches, enter exercise log data and generate feedback reports, and coordinate with the RTR executives to provide the email/text messages for the Reach Plus Messages group) and other key personnel. The analysis will include costs associated with the time required for intervention tasks and training but not research assessments (screening, randomization, questionnaires and other assessments). The research team has experience with developing time-tracking systems that capture information at the researcher level (CA 101770, B. Pinto, P.I.). Printing, postage and

telephone expenses will be tracked by setting up separate purchase order accounts for intervention materials and tasks. For participant costs, we will obtain information at 3, 9 and 12 months on the cost of exercise equipment, gym fees, and any medical expenses incurred by the participants for exercise-related injuries.

We will evaluate the impact of the intervention on QOL using the Short-Form-36 (SF-36) Health Survey. Questions about medical conditions will also be added to allow for case-mix adjustment of SF-36 scores. The SF-36 will be administered at baseline, 3, 9 and 12 months. The cost-effectiveness of our interventions will be estimated using the ratio of the difference in costs between Reach Plus Phone, Reach Plus Messages and Reach Plus to the difference in QOL and other outcomes at 12 months. The general equation for a cost-effectiveness ratio (CER) is:

$$CER = \frac{\sum_i \left(Cost_{intervention,i} - Cost_{usual\ care,i}\right)}{\sum_i \left(Effectiveness_{intervention,i} - Effectiveness_{usual\ care,i}\right)}$$

Where *i* is the *i*-th participant, cost is determined by resource utilization (as described above), and effectiveness is measured by QOL and quality-adjusted life-years (QALYs). QOL will be converted to health utilities, a measure of quality of life on a scale from 0 (death) to 1 (perfect health).[69] We will construct confidence intervals for our cost-effectiveness ratio using nonparametric bootstrapping.[70-72] Bootstrapping is a re-sampling technique that empirically estimates a sampling distribution for the cost-effectiveness ratio. Bootstrap samples are constructed by sampling the original data with replacement, with a sample size equivalent to the original data. The cost-effectiveness ratio is calculated using the mean cost and QALYs in the bootstrap sample. This process is repeated a large number of times (at least 1000 bootstrap samples are recommended) to estimate the sampling distribution of the cost-effectiveness ratio. A 95% confidence interval can be constructed by identifying the 26th least favorable and 975th most favorable cost-effectiveness ratios. The cost and QALY outcomes from each bootstrap sample will also be plotted on a cost-effectiveness plane.

F. Data Analyses

F.1. Preliminary analyses. We will assess potential between-group differences in baseline characteristics (socio-demographics, baseline exercise, mood, fatigue, QOL and physical functioning) using graphical methods, non-parametric and parametric tests as appropriate (e.g., Wilcoxin rank-sum test for skewed data, analysis of variance for normally distributed continuous data & chi-squared tests for categorical data). Any variables not balanced by randomization will be controlled for as covariates in subsequent analyses.

F.2. Primary Aim Analysis Plan. We will compare the three groups with respect to mean weekly minutes of MVPA (as measured by the 7-day PAR) at 3, *6*, 9 and 12 months (Primary Aim 1). To avoid the effect of outliers, we will apply a normalizing transformation (if necessary) to the outcome prior to analysis. A single linear mixed effects regression model will be used to simultaneously estimate the intervention effects (Reach Plus vs. Reach Plus Phone, Reach Plus vs. Reach Plus Messages and Reach Plus Phone vs. Reach Plus Messages) on MVPA at 3, *6*, 9, and 12 months, with a subject-specific intercept included to account for within-subject correlation in the outcome over time. We will control for baseline value of the outcome and potential confounders of treatment effects (including any variables not equally distributed between groups). Modeling is done using a likelihood-based approach and will make use of all available data (on the ITT sample) to obtain consistent estimates of the regression parameters. Finally, using Spearman rank order correlations, we will assess the agreement between self-reported (7 Day PAR) and objectively measured (accelerometer) MVPA.

F.3. Secondary Aims Analysis Plan (Aim 3). Using a similar analytic strategy to that described for the Primary Aim, we will assess potential between-group differences in fatigue, QOL, physical functioning and mood at 3, 9 and 12 months. A series of linear mixed effects regression models will be run (with subject-specific intercepts), to regress secondary outcomes at follow-up on intervention assigned, baseline values of the outcome and potential confounders (including any variables not balanced by randomization). Descriptive data will be maintained on any adverse effects associated with exercise participation by group (**Aim 4**).

F.4. Analysis Plan for Additional Exploratory Aims (Aim 5). Potential Moderators will be examined using similar linear mixed effects regression models, as those described above. For example, MVPA at 3, *6*, 9 and 12 months will be regressed simultaneously on the moderator (e.g., age), treatment assignment, and the interaction between the two. If the interaction term is nonzero, then we will conclude that there is evidence for a potential moderator. Models will also control for any potential confounders of the association, including baseline exercise and any variables unbalanced between groups. Given the limitations of our sample size, interest will be in exploring effect sizes to generate hypotheses about the potential differing effects of the interventions on exercise maintenance at follow-up. Potential Mediators of the intervention effects on MVPA at follow-up will be explored. Mediators of interest are self-efficacy, barriers to exercise and social support for exercise, as suggested by prior work.[73] Following Kraemer's approach,[74,75] a potential mediator must be in the causal path from intervention to outcome. For a variable M to be a mediator, we must show that (a) intervention assignment has a causal effect on M, and (b) M has a causal effect on the outcome. Testing condition (a) is more straightforward, as interventions are randomized. Since M is a post-randomization variable, testing condition (b) can be challenging. Our primary approach for testing potential mediators will be principal stratification.[76,77] This method can help estimate the causal effect of a post-randomization variable (such as a potential mediator M) on the outcome. We will compare these findings to that of more standard approaches.[78,79] Our sample size may not always provide sufficient power to simultaneously test for all possible mediators, but the individual mediation analyses will provide data for generating hypotheses about the mechanisms through which the intervention can impact exercise maintenance. Hence, our focus will not be on strict significance testing but rather estimating effect sizes and corresponding confidence intervals.

F.5. Missing Data Approaches. If a participant drops out, we will attempt to gather follow-up data. If women refuse to be contacted or lose contact with the study, we will censor the data at the point of loss. Our analyses will focus on the intent to treat (ITT) sample (all randomized participants will be included). The MIXED procedure in SAS 9.3 (which will be used for our primary and exploratory analyses) uses maximum likelihood (ML) approaches to produce estimates of the regression parameters. A ML approach makes use of all available data (e.g., does not drop a woman with missing 12-month data but observed baseline and 9-month data), without requiring imputation of missing values. ML estimates are consistent when missing data are related only to covariates and observed values of the outcome.[80] As it is possible (although not testable) that missingness may be related to the missing outcome, we will run a sensitivity analysis to explore the robustness of our results to various other assumptions of the missing data.

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