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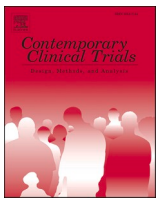

A multi-site trial of an electronic health integrated physical activity promotion intervention in breast and endometrial cancers survivors: MyActivity study protocol

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ABSTRACT

Despite the known benefits of moderate-to-vigorous physical activity (MVPA) for breast and endometrial cancer survivors, most are insufficiently active, interventions response is heterogeneous, and MVPA programming integration into cancer care is limited. A stepped care approach, in which the least resource-intensive intervention is delivered first and additional components are added based on individual response, is one strategy to enhance uptake of physical activity programming. However, the most effective intervention augmentation strategies are unknown. In this singly randomized trial of post-treatment, inactive breast and endometrial cancer survivors (n = 323), participants receive a minimal intervention including a Fitbit linked with their clinic's patient portal and, in turn, the electronic health record (EHR) with weekly feedback delivered via the portal. MVPA progress summaries are sent to participants' oncology team via the EHR. MVPA adherence is evaluated at 4, 8, 12, 16 and 20 weeks; non-responders (those meeting ≤80% of the MVPA goal over previous 4 weeks) at each timepoint are randomized once for the remainder of the 24-week intervention to one of two "step-up" conditions: (1) online gym or (2) coaching calls, while responders continue with the minimal Fitbit+EHR intervention. The primary outcome is ActiGraph-measured MVPA at 24 and 48 weeks. Secondary outcomes include symptom burden and functional performance at 24 and 48 weeks. This trial will inform development of an effective, scalable, and tailored intervention for survivors by identifying non-responders and providing them with the intervention augmentations necessary to increase MVPA and improve health outcomes.

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1. Introduction

There are 4.1 million breast cancer survivors and 890,000 endometrial cancer survivors in the US and this number continues to grow [1]. Increased moderate-to-vigorous intensity physical activity (MVPA) is associated with enhanced quality of life, reduced chronic disease risk, and improved cancer prognosis among survivors [2–12]. However, 70–90% fail to achieve [13] 150 min/week of MVPA as recommended by the American Cancer Society [14] and the American College of Sports Medicine [15]. Since referral to MVPA programs is not part of standard survivorship care and there are limited MVPA programs to refer to, few oncology providers refer survivors to MVPA programs [16], survivors have limited access to efficacious MVPA interventions. While oncology providers believe MVPA is important for cancer survivors, lack of available time for counseling or to set-up referrals and lack of available resources for referrals are cited as major barriers to providing energy balance interventions including MVPA to cancer survivors [16]. The design of existing MVPA interventions limits their potential for uptake as a referral source because they are resource-intensive, costly, and deliver multiple components (e.g., coaching calls, supervised exercise) simultaneously to all participants [17,18]. This "one-size-fits-all" approach often results in heterogeneity in response [19], does not address individual differences, and cannot be implemented into routine survivorship care due to cost and/or resource-intensity. Thus, there is a critical need for effective, scalable interventions that efficiently allocate resources to meet each survivor's needs.

An adaptive approach that implements lower-resource treatments (e.g., technology tools) for everyone first, and reserves higher-resource components (e.g., coaching) for survivors who fail to increase MVPA with low-resource treatments alone, offers a promising alternative to existing approaches because it: a) allows those with limited time or resources to participate and b) avoids providing high-resource components to those who respond to lower-resource interventions [19]. Integrating Fitbit MVPA data into the electronic health record (EHR; "Fitbit+EHR") with the capability to provide automated weekly progress feedback to participants via the EHR's patient portal represents a relatively low resource and potentially efficacious [20–23] minimal intervention that could be augmented as needed. The patient health portal ("patient portal") is an information technology (IT) tool that integrates with, or is tethered to, a healthcare system's HER and helps patients manage their health by providing access to health information, such as provider notes, test results, scheduling and messaging [24–29]. Fitbits can be linked with a patient's portal account to integrate patient-generated health data into a patient's medical record within the EHR, which is central to cancer care delivery. EHR integration signifies MVPA is important to survivors' health and enables a low-burden way for the cancer care team to support MVPA participation. Integration into the EHR can overcome some of the multi-level barriers to integrating MVPA in cancer care because it is low resource, allows for easy referral, doesn't depend on the oncology provider for delivery, and can provide oncology providers with easy to access counseling "scripts" tailored to each patient.

While the minimal Fitbit+EHR intervention will be sufficient for some survivors to increase their MVPA [23,30], others will need additional support [20,22,31,32]. Little data exists on what strategies would be most effective for augmenting a minimal intervention or when augmentation should occur. Some survivors may need more support at the start of a MVPA program whereas others may be able successful early on but struggle later as the amount of exercise prescribed increases and the novelty wanes. Thus, an adaptive intervention with a sequence of "treatment" decisions about which intervention components to deliver when could improve intervention efficacy and real-world uptake [33]. This trial employs an innovative singly randomized experimental approach [33] to determine optimal tactics to augment the Fitbit+EHR MVPA intervention for inactive breast and endometrial cancer survivors to inform adaptive intervention development.

2. Study aims

Fig. 1 provides a study design overview. The MyActivity study primary aim is to identify which of two predefined augmentation strategies for the Fitbit+EHR intervention leads to the greatest increase in MVPA at 24 and 48 weeks among breast and endometrial cancer survivors. The secondary aim is to identify the best augmentation strategy to improve symptom burden and functional performance at 24 and 48 weeks. We hypothesize non-responders to the Fitbit+EHR intervention will increase MVPA more and demonstrate more favorable symptom burden and functional performance at 24 and 48 weeks when randomized to coaching calls compared to the online gym resulting from the human support and accountability.

The MyActivity study will also explore baseline and time-varying moderators that influence MVPA, symptom burden and functional performance changes. Moderators to be examined include demographic and disease characteristics, symptoms (e.g., fatigue), functional status, self-efficacy, and intervention fidelity. These data will be used to develop a more dynamic, individualized but scalable intervention sequence that maximizes MVPA.

3. Materials and methods

3.1. Conceptual model

Social Cognitive Theory is a useful framework for designing MVPA interventions [34] because core determinants (self-efficacy, goal-setting, facilitators/ barriers, outcome expectations) and the mechanisms by which they work are specified [35]. Self-efficacy is posited to be related to increased intervention adherence and MVPA both directly and indirectly via facilitators and barriers (i.e., lack of facility access, social support), goal-setting/self-monitoring (i.e., monitoring MVPA, using feedback to measure progress), and outcome expectations (i.e., belief MVPA will result in a specific outcome). Fig. 2 details our conceptual model of how we hypothesize each intervention component impacts MVPA. Each component is designed to increase adherence and target multiple social cognitive theory constructs.

3.2. Study design

The MyActivity Study uses a singly-randomized trial, an efficient experimental approach to develop efficacious adaptive interventions, or multi-stage treatments that respond to the changing needs of individuals [33] (see Fig. 1). All participants receive the first-line Fitbit+EHR intervention. A standard weekly exercise prescription is used to gradually increase MVPA to 150 min/week by week 7 (see Table 1). Every 4 weeks (end of weeks 4, 8, 12, 16, and 20) for the initial 6-month intervention period, response to the intervention is assessed. Non-response is defined as meeting $<$80% of the cumulative MVPA goal for the previous four weeks. This criterion is designed to accommodate short-term adherence disruptions (e.g., illness, vacation, holidays). Those classified as non-responders are randomly assigned with equal likelihood for the remainder of the 24-week intervention period (ranging from 4 to 20 weeks) to one of two augmentation tactics: (1) online gym or (2) bi-weekly coaching calls (see Fig. 1). Randomization occurs only once per participant. Responders continue with the Fitbit+EHR intervention. For example, if a participant had a weekly goal of 150 min of MVPA for weeks 9 to 12 (600 min total), they must complete $\geq$480 min of MVPA to continue in the minimal intervention. If they engaged in $\geq$480 min, they would stay in the minimal intervention until the end week 16 where their response status would be evaluated again. If they did $<$480 min of MVPA during weeks 9 to 12, they would be randomized to the online gym or bi-weekly coaching calls. They would continue to receive their augmentation tactic for weeks 13–24 regardless of their goal attainment and would not be re-evaluated for response again.

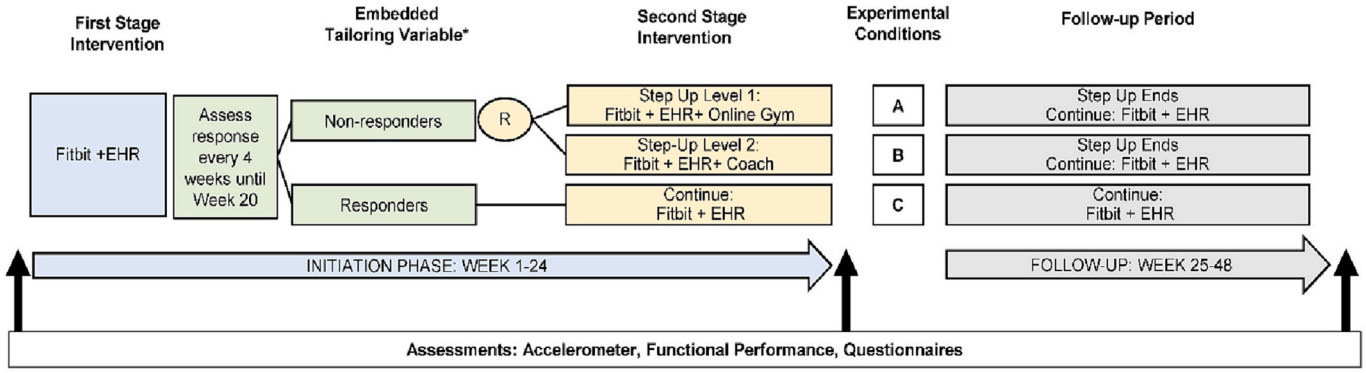
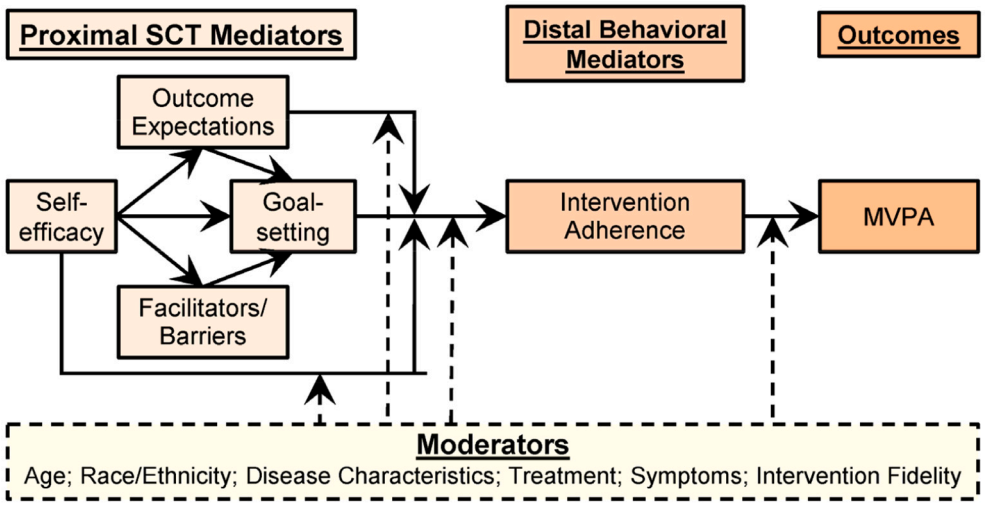


Fig. 1. MyActivity Trial design Provides a design overview of the study illustrating the interventional stages, follow-up period and timepoints for assessments.



Hypothesized mechanisms for each intervention component				
Intervention component	**Self-efficacy**	**Outcome expectations**	**Goal-setting**	**Facilitators/ barriers**
Fitbit + EHR	✓	✓	✓	✓
Online gym	✓		✓	✓
Coaching calls	✓	✓	✓	✓

Fig. 2. MyActivity Study Conceptual Model. This model details how we hypothesize each intervention component influences MVPA. SCT = Social Cognitive Theory; MVPA = moderator to vigorous physical activity; EHR = electronic health record.

At week 25, all participants will revert to receive only the Fitbit+EHR intervention during a 24-week follow-up maintenance period. During the maintenance period, those randomized to coaching calls no longer receive calls. For those randomized to the online gym, access to materials is maintained but all staff contact and provided schedules end.

3.3. Recruitment and screening

Inclusion and Exclusion Criteria. Eligibility criteria are: (1) female age ≥ 18 years, (2) ≤5 years since diagnosis of Stage I-III breast or Stage I-III type 1 endometrial cancer because cancer follow-up care is most frequent during this time; (3) ≥3 months since primary active treatment (completed surgery, chemotherapy, and/or radiation but endocrine or HER2-targeted therapies can be ongoing) completion; (4) self-report <60 min/week of MVPA; (5) able to access the internet daily on a computer, smartphone, or tablet; (6) have a patient portal account, or are willing to set up and use one; and (7) spoken and written English fluency. Exclusion criteria are: (1) absolute contraindications to exercise (i.e., acute myocardial infarction, severe orthopedic conditions), metastatic disease or planned elective surgery; (2) plans to become pregnant or to move from area, and (3) current enrollment in another dietary or activity trial. Participantion was restricted to.

Recruitment. Participants are recruited from two academic medical centers: the University of Wisconsin Carbone Cancer Center and Robert H. Lurie Comprehensive Cancer Center of Northwestern University which use the same EHR systems. Potentially eligible patients are identified using the EHR and invited to enroll. Invitations are primarily sent via postal mail with secondary recruitment via patient portal messages at the Wisconsin site and via email at the Northwestern site. The invitation includes study information and the URL for the REDCap-based eligibility screening questionnaire. Patients are followed up with a maximum of three times.

Table 1
MyActivity Study Exercise Prescription This table illustrates the gradual increase in MVPA to meet the goal of 150 min/week over the first seven weeks of the intervention. All participants receive this as a part of the Fitbit+EHR intervention. Non-response to this intervention is marked by meeting <80% of these weekly goals.

Week	MVPA goal (min/week)	Sessions per week	Session duration (mins)	Session RPE	Target heart rate (% of Max HR)
1	60	3–4	15–20	10–12	50–60%
2	75	3–4	20–25	10–12	50–60%
3	90	3	30	10–12	50–60%
4	105	3	35	10–12	50–60%
5	120	3–4	30–40	13–15	50–60%
6	135	3–4	30–45	13–15	60–75%
7+	150+	3–5	30–60	13–15	60–75%

Screening. The online screening questionnaire assesses study entry criteria and includes two safety screening instruments. The Physical Activity Readiness Questionnaire (PAR-Q) [36] assesses cardiovascular disease history, symptoms, risk factors, and other health issues. The Fall Risk Questionnaire [37] screens for falls risk factors. Eligible candidates are scheduled for a recruitment call and sent a study overview and copy of the informed consent. During the call, study staff review study details and confirm participants' eligibility and intent to participate. Participants complete informed consent and permission to contact physician forms, if needed, online via REDCap.

3.4. Intervention conditions

Minimal Fitbit + EHR Intervention. All participants receive a low-resource self-monitoring intervention consisting of two intervention components detailed below: MyActivity e-book and Fitbit. Participants connect their Fitbit to the MyActivity database, a secure, password protected database designed specifically for this study that is only accessible to study investigators, and the patient portal to transmit data to the study team in real-time and EHR, respectively. Following baseline assessment completion, an intervention kit including the Fitbit, detailed intervention information, exercise prescription, and instructions for Fitbit use is mailed. Participants attend a 30-min group study orientation via videoconference prior to study start date to review intervention tools and participation expectations. They are encouraged to set-up a one-on-one technology troubleshooting session as needed.

MyActivity eBook: This is a website containing educational information on MVPA, safety, MVPA benefits, how to effectively use the intervention tools, and provides education to target effective social cognitive theory behavior change strategies.

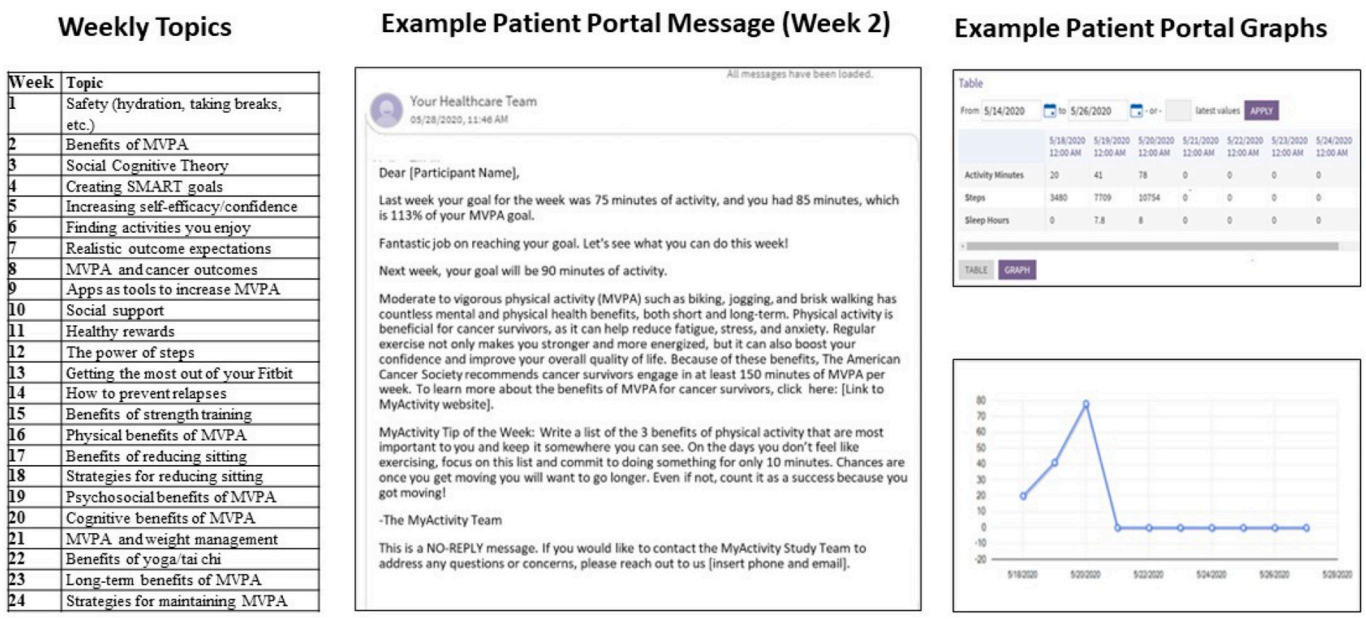
Fitbit + EHR. Participants are provided with a Fitbit Charge 3 and asked to download the Fitbit app and wear the Fitbit during all waking hours throughout the 48-week study period. The Fitbit measures activity intensity, steps, and heart rate, and syncs directly to the Fitbit app via a smartphone, tablet, or computer using Bluetooth or a provided dongle. The Fitbit and its associated app provide real-time notifications on progress toward weekly exercise goals. The Fitbit targets enhanced goal-setting and self-monitoring. At enrollment, an EHR order is placed, enabling the patient to link the Fitbit to the patient portal (MyChart) and thus, integrate Fitbit data with their EHR account. Data from Fitbit then automatically uploads into the EHR. Participants can view graphs of their weekly MVPA minutes and steps within their patient portal. They receive automated email notifications re-directing them to log-in to the patient portal to read their automated weekly progress message. Weekly progress messages are endorsed by the study and oncology care teams to convey the intervention is part of survivorship care and a priority of their care team. Weekly progress messages contain: a) weekly MVPA goal that is progressive to prevent injury and enhance self-efficacy via increasing mastery experiences., b) feedback on MVPA progress from previous week and month to enhance goal-setting and self-efficacy, c) encouraging messages tailored to goal attainment to enhance self-efficacy via social persuasion and d) strategies targeting social cognitive theory constructs to teach participants skills to enhance self-efficacy and goal-setting, overcome barriers, implement strategies to facilitate MVPA and develop realistic outcome expectations (see Fig. 3). Participants are encouraged to review and discuss progress messages at medical appointments with the oncology team. The oncology care team receives a) an automated EHR message with talking points to encourage MVPA tailored to the patient's progress on the morning of scheduled clinic visits and b) a monthly email summarizing each enrolled patient's study progress. The goal of these messages is to enhance clinician involvement while minimizing burden. Clinician involvement was specifically designed to enhance participant's self-efficacy via social persuasion.

Randomization of Non-Responders. Non-responders are randomized 1:1 using computer-generated randomly permuted block to one of two augmentation intervention components: (1) online gym or (2) bi-weekly coaching calls (see Fig. 1). Randomizations occur following week 4, 8, 12, 16 and 20. Participants are randomized once and remain in the augmented condition for the remainder of the 24-week intervention. To prevent bias, allocations are concealed as follows: 1) the two conditions are assigned a corresponding code and the key for this coding scheme is kept separate from randomization allocation and 2) randomization occurs automatically using concealed allocation sequence in the MyActivity database so randomization is blinded and not accessible to anyone other than the individual conducting randomization until allocation completion. To prevent purposeful faltering to receive augmentation strategies, participants do not know they may be randomized. The consent form describes the augmentations as intervention components they may be offered but does not specify conditions under which they are offered. Participants are notified of randomization via phone or email if they do not answer. The nature of the intervention precludes blinding of staff and complete blinding of participants. However, the statistician is blinded.

3.4.1. Augmentation interventions

Online gym. Participants randomized to the online gym receive a) a digital, "on demand" WalkStrong video library focused on walking and other cardiovascular activities to perform in the home with little/no equipment, b) exercise equipment (hand towel, 3 and 5 lb. hand weights), c) paper logs to track usage and d) a user guide and schedule for use. Videos were vetted by the research team for appropriateness and safety for cancer survivors with a range of ages and abilities. Each video includes an individual demonstrating a beginner, intermediate, and more advanced exercise version. A DVD is provided to those who request it. Online gym participants may attend an optional videoconference orientation for additional instruction. Participants are sent a weekly email to upload online gym logs and are called monthly to obtain missing logs. They are also provided with monthly feedback on online gym usage via email. The online gym was designed to facilitate access to MVPA resources.

Coaching Calls. Participants randomized to coaching calls receive 10–15 min semi-structured bi-weekly telephone calls delivered by trained research staff. Calls: a) provide feedback on previous two weeks' progress toward MVPA goals; b) review MVPA goals and personalized strategies for goal attainment over next two weeks; c) cover at least one social cognitive theory behavior change topic (i.e. building self-efficacy, setting realistic outcome expectations, overcoming barriers). Calls were developed to target self-efficacy, goal-setting, facilitators, barriers and outcome expectations.



Week	Topic
1	Safety (hydration, taking breaks, etc.)
2	Benefits of MVPA
3	Social Cognitive Theory
4	Creating SMART goals
5	Increasing self-efficacy/confidence
6	Finding activities you enjoy
7	Realistic outcome expectations
8	MVPA and cancer outcomes
9	Apps as tools to increase MVPA
10	Social support
11	Healthy rewards
12	The power of steps
13	Getting the most out of your Fitbit
14	How to prevent relapses
15	Benefits of strength training
16	Physical benefits of MVPA
17	Benefits of reducing sitting
18	Strategies for reducing sitting
19	Psychosocial benefits of MVPA
20	Cognitive benefits of MVPA
21	MVPA and weight management
22	Benefits of yoga/tai chi
23	Long-term benefits of MVPA
24	Strategies for maintaining MVPA

Fig. 3. Overview of the MyActivity Patient Portal Features. Participants receive a weekly patient portal messages with access to graphs of their progress; each week covers a different topic targeting social cognitive theory constructs.

3.5. Outcome measures

Participant assessments are conducted at baseline, 24 weeks, and 48 weeks (see Table 2 for full list). The primary outcome is accelerometer-assessed MVPA. Secondary outcomes include symptoms, functional performance, and social cognitive theory constructs. Demographic and disease characteristics are collected as potential moderators of MVPA changes. At baseline, participants are mailed an assessment kit including a) an accelerometer, accelerometer instructions, wear log, and postage-paid return mailer and b) a functional performance test kit with supplies and instructions for videoconferencing. Participants are instructed to wear the accelerometer for 7 consecutive days (see below for further detail) and to return the accelerometer to the study team via the provided postage-paid return envelope. Functional performance measures are conducted via videoconference by trained study staff (See Table 2 for details). At baseline, participants are instructed to put the functional performance test kit somewhere for safe keeping for re-use at 24 and 48 weeks. A personalized link to complete study questionnaires is emailed via REDCap. Participants receive reminders via phone or email to complete assessments. The same assessment procedures are followed at 24 and 48 weeks. Participants are incentivized for assessment completion ($20 at baseline, $30 at 6-months and $40 at 12 months) and permitted to keep the Fitbit.

Fitbit data are collected throughout the full study duration and are stored in the MyActivity Database.

Primary Outcome: MVPA. Physical activity is measured objectively and via self-report.

ActiGraph accelerometer. The ActiGraph accelerometer (Model GT3X-BT; ActiGraph, LLC, Pensacola, FL), a valid and reliable objective physical activity measure that provides no feedback to participants [38,39]. Participants are instructed to wear the monitor for 7 consecutive days on the non-dominant hip during all waking hours except when bathing or swimming. Activity data are collected at 30 Hz in 10-s intervals (epochs) to ensure granular data were collected for potential secondary analyses of any potential misclassifications or difference in outcome by epoch length but were reintegrated into 60s epochs for processing. Upon receipt, data are downloaded and assessed for valid wear time using ActiLife version 6.13.3 . If there is not ≥10 h/day of wear time on ≥5 days, participants are asked to re-wear the monitor. Data for wear periods ≥3 valid days at 24 and 48 weeks will be included in analyses. Average number of minutes of daily total activity and time spent in each activity intensity level (i.e. sedentary, light, moderate, vigorous) will be calculated using established cut points [40]. Minutes of moderate and vigorous activity are summed for a total measure of MVPA.

3.5.1. Secondary outcomes

Table 2 details secondary outcomes.

Self-Reported Physical Activity: The Godin Leisure Time Exercise Questionnaire (GLTEQ) [41] assesses self-reported times per week an individual typically engages in activity of three intensities (mild, moderate, and vigorous) and, within intensity, the typical activity session duration. The GLTEQ has demonstrated validity for assessing physical activity in breast cancer survivors [42,43].

Functional Performance. Measures include the 6-Minute Walk Test [44], the Short Physical Performance Battery (SPPB; [45–47]) and select items from the Senior Fitness Test (8-Foot Up-and-Go; 2-Minute Step Test and the Arm Curl test) [48]. Functional performance tests are conducted via videoconference which has been shown to be a valid and reliable method for remote administration of functional performance tests in older adults and cancer survivors [49–51].

Patient Reported Outcomes. Participants complete reliable, well-validated Patient-Reported Outcomes Measurement Information System (PROMIS) [52,54] self-report assessments of symptoms including fatigue, depression, anxiety, emotional support, pain interference, cognition, sleep and physical function, and the Functional Assessment of Cancer Therapy-Breast [53], a well-validated measure of QOL at each time point.

Social Cognitive Theory Constructs. All social cognitive theory constructs [55–59] are assessed including self-efficacy, goal-setting, outcome expectations, and barrier/facilitators. The measures used in this study have been validated and shown to be reliable for assessing social cognitive constructs in a multitude of populations.

Fidelity and Adherence. Adherence is evaluated throughout the intervention. See Table 2 for measures of fidelity and adherence to each intervention component. All measures are objectively obtained unless otherwise noted. Coaching calls are recorded for participants who consent to audio recording.

Feasibility and Acceptability. Fitbit+EHR intervention and additional intervention component's (online gym, coaching calls) feasibility (i.e.

Table 2
MyActivity Secondary Outcomes Measures All secondary measures of functional performance, patient reported outcomes, QOL, social cognitive theory constructs, fidelity and adherence to components and acceptability/feasibility are listed with details and timepoints for measurement.

Construct/Measures	Description	Time Point			
		Baseline	Week 3	Week 24	Week 48
Self-Reported Physical Activity					
Godin Leisure Time Exercise Questionnaire (GLTEQ) [39]	Measures self-reported weekly minutes of moderate and vigorous physical activity	✓		✓	✓
Functional Performance					
6-Minute Walk Test [44]	Measures submaximal functional capacity	✓		✓	✓
The Short Physical Performance Battery (SPPB) [45-47]	Includes timed measures of gait speed, ability to rise from a chair, and standing balance tests. Gait speed is measured using the better of two recorded times over a 4-meter course. Chair stand time is measured as the time needed to rise five times from a seated position in a chair with arms folded across the chest. Balance is measured by the participant's ability to stand in three positions (side-by-side, semi-tandem, and tandem) for 10 seconds each. Each measure is scored according to established cut points [45] and aggregated for a total SPPB score.	✓		✓	✓
Senior Fitness Test Items [48]	Measures include 8-Foot Up-and-Go, a test of physical agility and dynamic balance; the 2-Minute Step Test, an aerobic endurance test, which counts the number of full in-place steps completed in two minutes and the Arm Curl test, which assesses arm muscle strength endurance, specifically of the biceps Only participants who own a 5-pound dumbbell at baseline complete the arm curl test.	✓		✓	✓
Patient Reported Outcomes *[52]*					
PROMIS Physical Function Short Form 20a [52]	Measures functional limitations and interference over the past 7 days.	✓		✓	✓
PROMIS Fatigue Short Form 8a [52]	Measures frequency of fatigue symptoms and interference over the past 7 days.	✓		✓	✓
PROMIS Depression Short Form 8a [52]	Measures the frequency of a variety of depressive symptoms over the past 7 days	✓		✓	✓
PROMIS Anxiety Short Form 8a [52]	Assesses self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness) over the past 7 days	✓		✓	✓
PROMIS Applied Cognition-General Concerns Short Form 8a [54]	Assess the frequency of cognitive concerns over the past 7 days	✓		✓	✓

The PROMIS Sleep-Related Impairment Short From 8a [54]	Assesses participants' perceptions of sleep-related impairment over the past 7 days	✓		✓	✓
PROMIS Sleep Disturbance Short Form 8a [20] is	Assess participants' rating of overall sleep quality and perceptions of specific characteristics of sleep quality	✓		✓	✓
QOL					
Functional Assessment of Cancer Therapy-Breast [53]	Assesses participants' physical, social/family, emotional and functional well-being as well as breast cancer specific concerns	✓		✓	✓
Social Cognitive Theory Constructs					
Exercise Self-Efficacy Scale [55]	Assesses beliefs in ability to be physically active over the next 12 weeks	✓	✓	✓	✓
Barriers Self-Efficacy Scale [55]	Assesses beliefs in ability to be physically active over the next 12 weeks despite common barriers	✓	✓	✓	✓
Multidimensional Outcome Expectations for Exercise Scale [56]	Assesses social, self-evaluative, and physical outcome expectations for physical activity	✓	✓	✓	✓
Exercise Goal Setting Scale [57]	Assesses physical activity-related goal-setting, self-monitoring and problem Solving	✓	✓	✓	✓
Facilitator/Barrier: Social Support for Exercise Scale [58]	Measure physical activity support received from friends, family and other Survivors	✓	✓	✓	✓
Facilitator/Barrier: Physical Activity Enjoyment Scale [59]	Measures enjoyment and satisfaction with current physical activity program	✓	✓	✓	✓
Fidelity and Adherence to Intervention Components					
Minimal Intervention (Fitbit+EHR)	Average number of days Fitbit is worn; average number of weekly patient portal progress messages read by participant; total percentage of weeks MVPA goal met; proportion of EHR messages read by cancer care team	Ongoing →			
Coaching Calls	Total percentage of coaching calls attended; average time per call; fidelity to coaching call script	Ongoing →			
Online Gym	Average number of self-reported days used per week	Ongoing →			
Feasibility					
Participant Retention	Ratio of participants who drop out to participants retained in each component				✓
Safety	The number and severity of adverse events reported spontaneously and during non-spontaneous adverse event assessments. Acceptability is measured via a process evaluation to assess	Ongoing →			
Acceptability					
Process evaluation	Assesses intervention components' perceived effectiveness; b) plans to continue physical activity and intervention tool use; c) intervention elements liked/disliked; d) overall satisfaction with study experience and e) frequency of discussion with care team about physical activity and/or the *MyActivity* study			✓	✓

retention and safety) and acceptability (i.e. components' perceived effectiveness; intervention tool usage; satisfaction) are evaluated throughout the 24-week intervention, post-intervention (week 24) and at 48-week follow-up.

3.6. Other variables

Demographic and Disease Characteristics. Participants self-report demographic characteristics including age, race/ethnicity, marital status, education, income, and number of children. Additionally, participants report health status, cancer and treatment characteristics, height, weight, comorbid conditions, medications, and dietary information. Data pertaining to cancer and treatment is confirmed via the medical record.

COVID-19 related questionnaires. As enrollment began in November 2020, participants receive questionnaires to assess COVID-19 pandemic impact and adaptations.

3.7. Safety monitoring

This study has a data and safety monitoring board. Participants are instructed to report injuries to study staff within 24 h of occurrence. Additionally, they are emailed a personalized questionnaire every 8 weeks to report any adverse events that may have occurred but were not reported. We reach out to emergency contacts for participants who do not have any data for $\geq$14 days and have not responded to contact attempts during that period to re-engage and ensure safety.

3.8. Privacy and confidentiality

To protect participant privacy, no personal information is stored or associated with their MyActivity database account. All Fitbit data transmitted via the MyActivity database are collected using the Northwestern University server cluster, which has limited physical access, is firewalled, and is regularly monitored for security issues. All phone encrypted data transmissions use a secure sockets layer protocol with a unique token for each participant. All data are backed up regularly. Any personal health information and Health Insurance Portability and Accountability Act data are stored on separate data clusters with unique keys and limited firewalled access. The study consent form details potential privacy and confidentiality risks and practices implemented to ensure protection.

3.9. Data analytics plan

All participants will be included in the intent-to-treat sample. Every effort is made to collect all outcome measures even if a participant does not engage in assigned treatments. Analyses will be conducted in SAS 9.4 (SAS Institute, Inc., Cary, NC).

Aim 1 and Aim 2 Analyses. All subjects are included in the primary analyses. The primary aim is a comparison of accelerometer-assessed weekly MVPA minutes between the coaching augmentation strategy (all of the responders + the subset of non-responders randomized to coaching) and the online gym augmentation strategy (all of the responders + the subset of non-responders randomized to online gym). Linear mixed models (LMM; [60]) using SAS PROC MIXED will be used to analyze the longitudinal data. LMMs use all available outcome data, allowing subjects to have an unequal number of observations, and accommodating missingness when data are missing at random. The LMM will include fixed effects for the intercept, time, group term, and a group-by-time interaction term. The group indicator will be defined as online gym or responder vs. coach or responder. The LMM also will include random effects for the intercept and time (to account for within-person correlation). Model diagnostics will be used to determine the suitability of more parsimonious (e.g., autoregressive) correlation structures, and nonlinear effects for time. From the fitted LMMs, the primary hypothesis will be examined by testing if the coefficient of the group-by-time interaction term, the difference in slopes between online gym or responder and coach or responder, is different from zero. These same analyses will be repeated for each of the symptom burden and functional performance outcomes in Aim 2. Secondary subgroup analyses will be conducted based on time of randomization to examine whether time in the augmented intervention influences outcomes.

Exploratory Aim(s). These analyses will explore baseline (i.e. demographic, disease characteristics, social cognitive, health status, physical function) and time-varying (e.g., adherence to wearing the Fitbit, changes in self-efficacy) moderators of participation in MyActivity, overall, and the effects of the different interventions (online gym, coach, or responder) received on MVPA, symptom burden and functional performance changes at 24 and 48 weeks. For theses assessments, the LMMs for the primary and secondary analyses of efficacy will be expanded to include the three-way interaction between the potential moderator, group and time.

Sample Size and Power. Sample size for this study is based on our primary aim which is a comparison of weekly accelerometer-assessed MVPA minutes among non-responders randomized to the online gym relative to those randomized to coaching calls at 24 and 48 weeks. Based on preliminary data [61], we assumed an overall SD of 110 min/week and an attrition rate of 10%. Enrolling 320 participants would result in 172 sub-optimal responders after attrition. By assuming a non-response rate of 60%, we estimate, 86 participants will be randomized and retained in each augmented condition. Thus, we will have >80% power for detecting a small to moderate effect size (Cohen's $d = 0.31$) between the two augmentation tactics for non-responders.

4. Discussion

Early detection and treatment advances have resulted in a large, growing, population of breast and endometrial cancer survivors, a trend expected to continue over the next decade [1]. MVPA interventions may attenuate negative treatment-related side effects and improve health and disease outcomes [2–12]. However, most breast and endometrial cancer survivors remain insufficiently active [13]. The majority of existing MVPA interventions employ a one-size-fits all approach whereby multiple intervention components are delivered simultaneously and do not adapt to performance, even if MVPA goals are not being reached. This means that once an individual struggles, they likely remain unsuccessful. The one-size-fits all approach disregards individual differences or yields an unscalable intervention package, impeding widespread intervention uptake.

The MyActivity study is designed to provide evidence for an adaptive approach to increasing MVPA that conserves resources by allocating more costly intervention components only where needed. This approach is efficient and consistent with clinical practice where treatment dose is based on individual response. An adaptive approach using technology tools, like the ones used in MyActivity, allows the intervention dose to change based on performance to increase individuals' chances of success [33]. This design has potential to provide the right intervention to the right person when they need it, improving health outcomes. MyActivity explores not only which adaptive approach is most efficacious, but also what factors moderate these effects. Further, integration within oncology care may enhance the chances of success. Ultimately, data from this study will inform dissemination and implementation of MVPA interventions in cancer care.

This study is not without limitations. First, although we assess adherence at multiple time points, participants can only be randomized once, and all randomizations occur during the 24-weeks initiation period. Some individuals may still benefit from additional or different augmentation strategies if the first line strategy is not effective, and others may need augmentation at additional time points during initiation or during the maintenance period. Other components we are not testing could be more effective as augmentation strategies for increasing

MVPA. However, we are only able to test a finite number of components given budgetary and resource constraints (limitations of all studies). Additionally, we are not specifically tailoring our intervention to survivors' demographic or disease characteristics. However, data from this study could be used to identify potential moderators of the intervention components to determine whether future tailoring is warranted. Finally, the study requires some level of technology knowledge/access (e.g., owning a smartphone or having a patient portal account) to participate, which excludes individuals without these resources. Despite these limitations, this is one of the first studies to test an adaptive MVPA promotion intervention that is integrated into cancer care and will provide fundamental knowledge on how to move research in this area forward.

MyActivity represents the first systematic effort to develop an adaptive MVPA intervention for any cancer population. Knowledge gained from this study will inform the development of effective, scalable, clinic-based interventions to improve quality of life and reduce disease burden among breast and endometrial cancer survivors. Ultimately, this work will significantly contribute to understanding how to effectively increase and maintain MVPA to improve health and disease outcomes in cancer survivors.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Amye J. Tevaarwerk Epic Systems- family member.

Data availability

No data was used for the research described in the article.

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