PROTOCOL TITLE: Technology Supported Physical Activity Intervention for Metastatic Breast Cancer Survivors: Fit2ThriveMB (Fit2ThriveMB)

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Indicate Vulnerable Population(s) to be Enrolled	☐ Children ☐ Cognitively Impaired Adults ☐ Pregnant Women (IF the research activities will affect the pregnancy or the fetus) ☐ Prisoners (or other detained/paroled individuals)
International Research (check this box if you will collect data from individuals located outside the United States)	☐
Research involving external collaborators (some research activities will be carried out by individuals not employed by Northwestern or NU affiliates)	☐
Research has U.S. Federal government funding (e.g., NIH, NSF, other federal agencies/departments)	☒

1.0 Purpose of the study:

The number of women diagnosed with metastatic breast cancer (MBC) is expected to increase by 31% in the next 10 years. Further, treatment advances have resulted in a doubling of 5-year survival rates in the last two decades to 36%, and 11% survive ≥10 years.[1] Thus, the population of women with MBC is growing. Women with MBC have higher rates of physical impairments,[2] greater symptom burden,[3] and lower levels of fitness and strength[3, 4] than early stage survivors and non-cancer controls resulting in compromised quality of life (QOL). Interventions are needed to alleviate adverse health effects and allow MBC patients to function optimally in the years they survive with advanced cancer. However, few health-enhancing interventions exist for women with MBC, and only 2-5%[5] of research funds for breast cancer are spent on metastatic disease despite high morbidity rates. Thus, research in women with MBC is desperately needed.

Increased physical activity (PA) is consistently associated with fewer treatment-related side effects, higher QOL, increased survival and reduced recurrence and mortality[6-9] among early stage survivors. Increasing light intensity PA and reducing time spent sedentary may also reduce functional decline,[10] improve QOL and QOL[11, 12] and body composition[13] and reduced mortality[14] independent of more intense PA. However, there is a paucity of research on PA in MBC patients. Two out of the three existing interventions in MBC patients[15, 16] were deemed not feasible due to their focus on intense PA and/or requiring on-site visits. Thus, PA interventions which use mobile health (mHealth) technology may be particularly useful for these women because they allow for remote monitoring of patients which facilitates individual tailoring of PA programs to patient's abilities and do not require travel to on-site, supervised PA sessions, reducing participant burden. However, no studies have examined effects of a mHealth intervention on PA in MBC patients. The proposed study seeks to address these critical research gaps by testing a highly tailored, remotely delivered mHealth intervention to promote PA of any intensity (i.e. light, moderate or vigorous) via increasing daily steps in MBC patients. This approach may have substantial health benefits for MBC patients, facilitate gradual and safe adoption of more intense PA and be more achievable than high volumes of more strenuous PA. [17, 18]

The primary purpose of the present study is to pilot test the feasibility and acceptability of a 12 week remotely delivered mHealth intervention to increase PA in MBC patients using a two-arm randomized control trial (RCT). We will also examine the effects of the intervention on symptom burden, QOL and functional performance, important outcomes in MBC patients. Inactive MBC patients (n=50) will be assigned to *Fit2ThriveMB* or education control. Participants assigned to the *Fit2ThriveMB* will receive the *Fit2ThriveMB* smartphone app, Fitbit, and coaching calls. Participants in the education control will receive educational materials and calls during the intervention period and the Fitbit following completion of 12 week assessments. The proposed study represents the first systematic effort to test a mHealth intervention to increase PA in MBC patients. This study addresses a critical research question related to PA and cancer survivorship (i.e. Is there a role for PA in advanced cancer?)[19] and supports NCI's research priorities of creating more feasible mHealth PA interventions for survivors.[11] Findings from this study will provide essential knowledge to help understand the health benefits of increasing PA in MBC patients. Specific aims are:

Aim 1. To pilot test the feasibility and acceptability of *Fit2ThriveMB,* a 12-week mHealth PA intervention in MBC patients (n=50) in a two-arm RCT (*Fit2ThriveMB* vs. education control). We hypothesize the following: a) ≥80% of MBC patients will be retained in the intervention; b) enrollees will set an individualized PA goal, adhere to their goals and wear the Fitbit on ≥70% of study days and c) ≥70% of participants will rate the intervention as acceptable.

Aim 2. To examine the potential effects of *Fit2ThriveMB o*n PA. MBC patients in *Fit2ThriveMB* will demonstrate greater increases in PA as measured by average daily accelerometer-assessed steps and time spent in any activity intensity (light, moderate or vigorous) than education controls at 12 weeks.

Aim 3. To examine outcome patterns suggesting the efficacy of *Fit2ThriveMB* for improving symptom burden (i.e. fatigue, depression, anxiety, pain, and physical function), functional performance and QOL

compared to education control. MBC patients in *Fit2ThriveMB* will demonstrate more favorable symptom profiles, functional performance and QOL than controls at 12 weeks as measured by well-validated standardized measures.

The proposed study is the first to test the effects of a mHealth intervention to increase PA in MBC patients. The proposed study will inform a fully-powered R01 by providing insight into: a) feasibility and acceptability of *Fit2ThriveMB* and b) preliminary effect sizes for PA, symptom burden, functional performance and QOL. Ultimately, the proposed study will provide key evidence to support the feasibility, acceptability and health benefits of increasing PA in MBC patients using a scalable intervention strategy that could be easily integrated into care to improve health and disease outcomes.

2.0 Background / Literature Review / Rationale for the study:

Increased incidence and life expectancy has resulted in a growing population of metastatic breast cancer (MBC) patients. [1] MBC patients have poorer quality of life (QOL) and higher rates of functional decline and premature mortality compared to early stage survivors and healthy controls.[2-4] Interventions are needed to alleviate adverse health effects and allow metastatic patients to function optimally in the years they survive with advanced cancer. However, few health-enhancing interventions exist for women with MBC. Increased physical activity (PA) is consistently associated with fewer treatment-related side effects, higher QOL, increased survival and reduced recurrence and mortality among early stage survivors.[6-9] Increasing light intensity PA and reducing time spent sedentary may also reduce functional decline,[10] improve QOL and QOL[11, 12] and body composition[13] and reduced mortality[14] independent of more intense PA. However, there is a paucity of research on PA in MBC patients, and existing interventions have been deemed not feasible due to their focus on intense PA and/or requiring on-site visits. mHealth PA interventions may be particularly useful for these women because they allow for remote monitoring of patients which facilitates individual tailoring of PA programs to patient's abilities and do not require travel to on-site, supervised PA sessions, reducing participant burden. Yet, no studies have examined a mHealth PA intervention in MBC patients. We propose to address these critical research gaps by testing a highly tailored technology-supported intervention to promote PA of any intensity (i.e. light, moderate or vigorous) via increasing daily steps in MBC patients. This approach may have substantial health benefits for MBC patients, facilitate gradual and safe adoption of more intense PA and be more achievable than high volumes of more strenuous PA. [17, 18] The primary aim of this study is to pilot test the feasibility and acceptability of a 12 week technology-supported intervention to increase PA in inactive MBC patients (n=50) using a two-arm randomized control trial (Fit2ThiveMB versus education control). The Fit2ThriveMB intervention consists of a Fitbit, coaching calls and the Fit2ThriveMB smartphone app which provides self-monitoring, a tailored goal-setting tool, real-time tailored feedback, app notifications, and a group message board. We will also examine outcome patterns suggesting the efficacy of Fit2ThriveMB on symptom burden, QOL and functional performance, important outcomes in MBC patients compared to the education control. The primary outcome time point is post-intervention 12 weeks. This project is significant because it will provide essential evidence to support the feasibility, acceptability and health benefits of increasing PA in MBC patients using a scalable intervention strategy that could be easily integrated into care to improve health and disease outcomes in this population.

3.0 Inclusion and Exclusion Criteria:

Inclusion criteria:

- Female; ≥ 18 years of age
- Diagnosed with metastatic breast cancer or locally advanced disease not amenable to surgical resection (Metastases to the auxiliary lymph nodes, and nowhere else in the body, do not qualify).
- Fluent in spoken and written English
- Own a smartphone
- Have access to the internet to complete assessments

- Self-report engaging in <150 minutes of moderate to vigorous PA per week.

Exclusion criteria:

- Untreated brain metastases
- Breast cancer with metastases to only the auxiliary lymph nodes.
- Uncontrolled cardiovascular disease or other major contraindications (i.e. non-ambulatory, severe cognitive or functional limitations) to PA participation
- Current enrollment in another dietary or PA trial

All MBC patients must obtain medical clearance from their oncologist to participate.

Adults unable to consent/Cognitively Impaired, individuals who are not yet adults (under 18 years of age), pregnant women and prisoners or other detained individuals will NOT be included in the present study.

4.0 Sample Size:

We will recruit 50 metastatic breast cancer patients to participate in this study. Sample size calculations (n=50) are based on the successful completion rate defined as: a) an attrition rate of ≤20% (i.e. complete 12 week assessment) and b) adherence to daily goals and wearing Fitbit ≥70% of study days (i.e. ~59/84 days). With half of participants (n=25) assigned to each condition, there is >85% power to differentiate between a 60% (control) and 80% (*Fit2ThriveMB*) "successful completion" rate with a one-tailed, exact test for binomial proportion at a 0.05 significance level (SAS V9.4).

5.0 Recruitment and Screening Methods:

Participants will be recruited from the following sites, all affiliated with Northwestern University Feinberg School of Medicine and the Lurie Comprehensive Cancer Center, or additional Northwestern Medicine sites : a) outpatient facility at Galter Pavilion of Northwestern Memorial Hospital; b) Lynn Sage Comprehensive Breast Cancer Center at Prentice Women's Hospital; and c) additional Northwestern Medicine Cancer Center locations (e.g. Cancer Center at Northwestern Medicine Lake Forest Hospital, Northwestern Medicine McHenry Hospital Cancer Center, Northwestern Medicine Cancer Center Delnor). For all methods, we will consult with patient's oncologists on an as needed basis to help determine if potential patients are good potential candidates for participation.

Screening

Participants will complete initial eligibility screening online or over the phone. It will take approximately 15 minutes. Screening will include evaluation of eligibility, the Physical Activity Readiness Questionnaire (PAR-Q)[20], which assesses cardiovascular disease history, symptoms, risk factors, and other health issues and the Fall Risk Assessment Questionnaire (FRQ)[21], which identifies individuals who may be at risk for falling. Screening will also include questions regarding technology and equipment the women currently have at home that may be usable for the baseline and week 12 functional performance video conference assessments. All women will also be required to obtain medical clearance from their oncologist.

Method 1: Recruitment Emails. The Northwestern Enterprise Data Warehouse (NMEDW) NMEDW (https://www.nucats.northwestern.edu/resources/data-science-and-informatics/nmedw/index.html) was designed to create a single, comprehensive and integrated repository of all clinical and research data sources on the campus to facilitate research, clinical quality, healthcare operations and medical education. We will use the NMEDW to obtain lists of NU patients who have agreed to be contacted regarding research study opportunities at Northwestern University and meet gross eligibility criteria with respect to diagnosis. We have also obtained an exception to view the clinic schedule in EPIC to compliment the NMEDW list. Patients who have come in for a visit recently, who meet the eligibility requirements, will be identified through this schedule. In addition, we have been granted access to oncologist's schedules via the exception process. Potential participants recruited through the NMEDW or clinic schedules will be e-mailed a letter notifying them about the study. This email will also contain a link to complete the

online screening housed in REDCap if they are interested in participating. If an individual does not want to participate, they will be asked to simply indicate this by responding to the e-mail. If we do not hear from the patient within 3-5 business days, we will follow-up with additional phone or email contacts, but will not exceed three attempts. If at least 6 months pass following the initial recruitment attempt with no response from the patient, an additional, single recruitment attempt may be made via phone call and/or email.

Method 2: Physician Referral. Clinicians will be encouraged to discuss the study with their patients. If her physician discusses the study with her and she agrees to have them send study staff her name, we will either e-mail her a description of the study and a link to complete the on-line screening, or follow-up with a phone call. If we do not hear from the patient within 3-5 business days, we will follow-up with additional contacts via telephone call or e-mail, but will not exceed 3 attempts.

Method 3: Self-Referral. If an individual contacts the researcher and is interested in participating in the study, s/he will be screened over the phone or online. The Study Coordinator will also work with the clinical team to confirm eligibility and appropriateness for the study. Subjects may self-refer to the study after hearing about it via clinic flyers, word of mouth, or via the media/NU newsletters if the principal investigator is interviewed.

6.0 Research Locations:

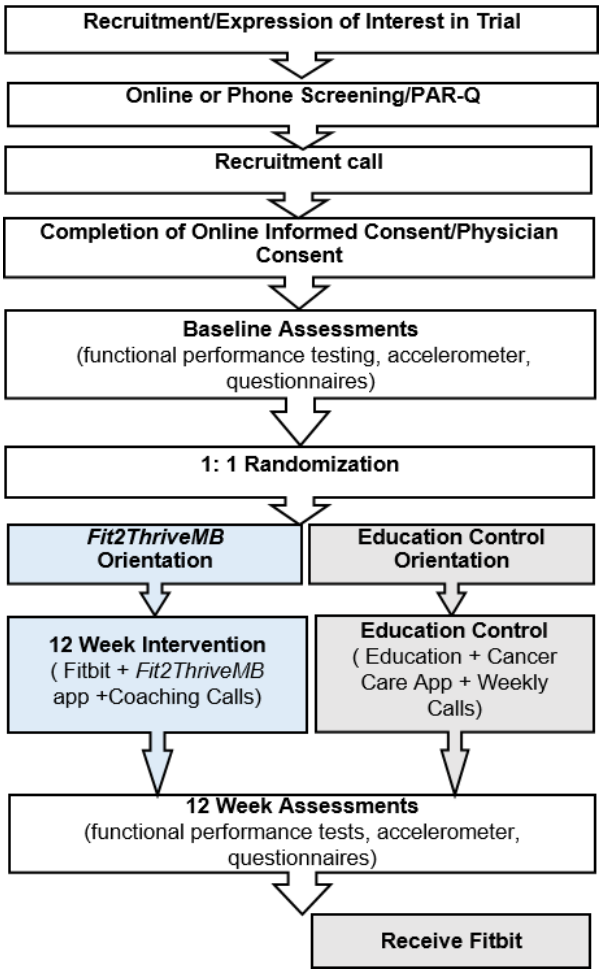
Research procedures will take place in the Department of Preventive Medicine at Northwestern University Feinberg School of Medicine.

7.0 Multiple sites: N/A

8.0 International Research: N/A

Fig 1. Participant Flow Through Study

9.0 Procedures Involved:



Study Design

This study uses a two-arm randomized control trial to promote physical activity in insufficiently active metastatic breast cancer patients (n=50). Participants will be randomized 1:1 to either the *Fit2ThriveMB* technology supported physical activity promotion intervention (*Fit2ThriveMB* app + Fitbit + coaching calls) or the education control (cancer.net app + phone calls). The primary outcome measurement is post-intervention (12 weeks). The flow of participants through the study is detailed in **Figure 1**.

COVID-19 Pandemic Procedures

A group of 13 women completed all screening, recruitment and consent, but no other study-related procedures in February and March 2020 with the intention to participate in wave 2 of the study, which was to begin in April 2020. Due to the COVID-19 pandemic, further recruitment for wave 2 and the start date for wave 2 was delayed indefinitely. Participants were notified of the delay in April 2020. Because the study procedures have changed substantially, and whether these participants meet the study eligibility criteria may have changed (i.e. they may be too active or have had their cancer metastasize further), we have determined it is best to un-enroll these women, and give them the option to re-enroll as new participants when recruitment resumes. Thus, once recruitment re-starts, these 13 patients will be notified they have been un-enrolled and contacted to complete screening and recruitment procedures a second time (i.e. screening survey, recruitment phone call, and sign informed consent and physician consent) in order to ensure that these participants remain eligible to participate and understand changes made to the study protocol.

Screening

Participants will complete initial eligibility screening online or over the phone. It will take approximately 15 minutes. Screening will include evaluation of eligibility and the Physical Activity Readiness Questionnaire (PAR-Q)[20], which assesses cardiovascular disease history, symptoms, risk factors, and other health issues, the Fall Risk Assessment Questionnaire (FRQ)[21], which identifies individuals who may be at risk for falling, and questions relating to technology and supplies that may be used for at-home functional performance video conferences. All women will also be required to obtain medical clearance from their oncologist.

Recruitment-phone call

All women who are eligible and indicate interest after the online or phone screening survey will receive a recruitment call. Before making the recruitment call, study staff will double check participant's medical records to be sure their cancer diagnosis is eligible for the study. During this call, study staff will explain the study in greater detail, and will confirm cancer stage and metastasis. There will be a final check for cancer stage following the call. If the participant is still interested and eligible, they will be sent a link to the online version of the informed consent and a copy of the permission to contact physician so physician consent can be obtained. If the potential participant screens via phone the content of the recruitment call will be completed as part of the screening phone call.

Assessments

Those who are eligible, agree to participate, provide informed consent, and provide physician consent will be: a) scheduled for a functional performance testing video conference with study staff via Zoom; b) sent an email with an individual, secure link to study questionnaires via REDCap and c) notified an accelerometer has been mailed. Participants will be asked to complete questionnaires within 1 week of receipt. MBC patients will be provided with detailed written instructions for wearing the accelerometer and directed to wear the monitor on specified dates attached to on the non-dominant hip during all waking hours, except when bathing or swimming, for 7 consecutive days and return the monitor and monitor log to the study team through the mail using a postage paid envelope provided by the study team. The questionnaires will take approximately 30-45 minutes to complete. The functional performance video conference will consist of completion of remote, individual functional performance testing (see Measures). In addition to the accelerometer and accelerometer instructions, participants will be mailed a remote functional performance testing kit that will include equipment required to complete the testing (i.e. blood pressure cuff, pedometer, hand weight, rope pre-measured for test distances, digital scale). The functional performance testing video conference will last from 60-90 minutes. Procedures will be the same at baseline and 12 weeks. Participants will be asked to hold onto the functional performance testing kit for the 12 week study so materials can be used at baseline and 12 weeks and will be provided with a postage paid box to ship materials back to the study team at week 12. At 12 weeks, the control group will participate in a virtual functional performance testing session and an optional virtual brief orientation to the app and Fitbit . The intervention group will participate in video conference functional performance testing and a study information and feedback session, which may occur via group video conference, or an individual phone call or video conference. Participants in the intervention group will also be provided with instructions for how to delete the Fit2ThriveMB app at the conclusion of the 12-week intervention. In addition, all participants will be asked to complete a short questionnaire battery during week 3 that will take approximately 10-15 minutes to complete.

Randomization and Orientation

After remote functional performance testing is complete, assessment materials (i.e. accelerometer, activity wear log, etc.) are received in the mail by study staff, and all data are verified, MBC patients (n=50) will be randomized 1:1 to *Fit2ThriveMB* intervention or education control group using computer-generated randomly permuted blocks. Individuals randomized to the *Fit2ThriveMB* intervention group will receive all intervention materials in the mail, and will participate in a remote, group or individual (depending on scheduling conflicts) orientation via Zoom video conference which will consist of instructions on all intervention procedures and assistant with downloading and setting up the *Fit2ThriveMB* app, Fitbit and Fitbit app. MBC patients assigned to the education control will also receive all control group materials via mail and will participate in a remote, group or individual (depending on scheduling conflicts) orientation session via Zoom video conference, during which they will receive instructions on study procedures and assistance with downloading and setting up the Cancer.Net app. Individuals in the control group will be informed they will receive the Fitbit after completion of 12 week assessments. The study orientation video conferences will take approximately 60-90 minutes. As in our previous studies, participants will start the intervention in cohorts of 6-12 individuals per condition to ensure an adequate number of participants for the *Fit2ThriveMB* message board.

Intervention Components

***Fit2ThriveMB* Intervention**

The *Fit2ThriveMB* intervention will consist of the Fitbit, *Fit2ThriveMB app,* and weekly coaching calls that will last from 10-15 minutes each. **Table 1** provides an overview of the weekly schedule of content for the intervention.

Table 1. *Fit2ThriveMB* Weekly Schedule of Intervention Content

Week	Theme	Daily Goal Setting	Daily Symptom Report	Tailored Push Notifications	Weekly Coaching Call
1	Intro to coaching calls/Getting started/SMART Goals	Yes	Yes	2-3/day	Yes

2	Benefits Reducing Sitting and Overcoming Barriers to Reducing Sedentary Behavior	Yes	Yes	2-3/day	Yes
3	Benefits of Increasing PA and increasing steps	Yes	Yes	2-3/day	Yes
4	Finding Activities You Enjoy	Yes	Yes	2-3/day	Yes
5	Self-monitoring	Yes	Yes	2-3/day	Yes
6	Managing symptoms	Yes	Yes	2-3/day	Yes
7	Overcoming barriers	Yes	Yes	2-3/day	Yes
8	Increasing Self-Efficacy	Yes	Yes	2-3/day	Yes
9	Realistic Outcome Expectations	Yes	Yes	2-3/day	Yes
10	Social Support	Yes	Yes	2-3/day	Yes
11	Healthy Rewards	Yes	Yes	2-3/day	Yes
12	Relapse Prevention	Yes	Yes	2-3/day	Yes

Intervention components include:

Fitbit

MBC patients will be provided with the Fitbit InspireHR). They will be asked to download the Fitbit app and wear the Fitbit 24/7 throughout the 12 week study period. The Fitbit measures PA intensity, steps, and heart rate and syncs directly with the smartphone and will automatically sync with the *Fit2ThriveMB* app and provide Fitbit data to the study team in real-time.

***Fit2ThriveMB* App**

The *Fit2thriveMB* app will encourage MBC patients to increase their PA via increasing their step count. Patients will be provided with educational information on PA and effective behavior change strategies for incorporating more PA into their daily lives to increase their step count (i.e. 10 minute lunch time walk, parking further from entrances, pacing while on the phone, etc.). Participants will be prompted each morning to report the intensity of their symptom burden (0 to 5). Based on their symptom rating and their previous day's step counts, MBC patients will be provided with three different options or levels of goals for that day to either increase or decrease 10-20% or remain constant, depending on symptom burden and previous day's progress as measured by the Fitbit (see **Table 2** for example options). The first day's PA goal-setting options will be based on that day's symptom reporting and their Actigraph PA data from baseline assessments. If they fail to choose a goal, they will be provided with the middle level goal as their goal for the day. Participants will be instructed to self-monitor progress towards these goals via the feedback on Fitbit Inspire HR monitor and the daily, weekly and monthly progress information provided in the *Fit2ThriveMB* app. The app will send MBC patients 2-3 reminders, encouragement or real-time PA feedback messages each day. These messages will be tailored to Fitbit PA data and reported symptom burden. Similar messages and tailoring strategies have been used in Dr. Phillips' *Fit2Thrive* study and Dr. Spring's ongoing NIH-funded behavior change studies (R01DK097364/R01DK108678). Finally, participants will have access to a message board where they can communicate with other MBC patients in the intervention to provide encouragement and support. Participants will have a profile where they can opt to share information including their first name, a self-portrait, their age, hobbies, favorite activities, motivation for becoming more active, goals for participating in the program, and favorite quote. Each participant's relative progress toward their daily goal (i.e. a circle that fills in as they meet their goal) will be

Table 2. Example Daily Step Goal Logic

IF MET PREVIOUS DAY'S STEP GOAL =…	AND SYMPTOM BURDEN IS…	THEN DAILY STEP GOAL OPTIONS ARE:
YES	LOW	1) Stay the same 2) Increase 10% 3) Increase 20%
YES	MODERATE	1) Decrease 10% 2) Stay the same 3) Increase 10%
YES	HIGH	1) Decrease 20% 2) Decrease 10% 3) Stay the Same
NO	LOW	1) Decrease 10% 2) Stay the same 3) Increase 10%
NO	MODERATE	1) Decrease 20% 2) Decrease 10% 3) Stay the Same
NO	HIGH	1) Decrease 20% 2) Decrease 10% 3) Stay the Same

posted at the top of the message board and all members will receive a notification when a member reaches their daily goal to facilitate encouragement and support from the group. This board will be closely monitored and facilitated by study staff to enhance use and prevent misuse.

Though not part of the intervention, participants may choose to keep the *Fit2thriveMB* study app on their phones and continue to use it. The functionality of the app depends on data collection. Data will continue to be collected after the conclusion of the 12 week intervention if a participant chooses to keep and use the app. Data collected includes: login frequency, app usage, data entered into the app including symptom burden, goal selection and physical activity and data transmitted from the Fitbit, including physical activity and steps taken. The app will remain functional and data will be collected for 12 months after the participant completes the initial 3 month intervention. The data is collected and stored for the purpose of analyzing post-intervention app usage and physical activity patterns. At the end of 12 months the app will no longer function. Participants will be provided with written instructions on how to remove the app if they wish during the 12 week functional performance video conference. Once the app is removed we will be unable to collect any data from their phone.

Coaching Calls
Fit2ThriveMB intervention participants will receive weekly coaching calls which will: a) provide feedback on the previous week's symptom burden and progress on PA goals; b) review personalized goals and strategies for increasing PA for the next week; c) provide instruction on effective behavioral change techniques (see **Table 1 for listing of topics to be covered**) and d) inquire about any issues or injuries. Participants will be instructed to call or email their coach throughout the week if they encounter any issues. Coaching calls will be semi-structured and recorded to ensure fidelity. Coaching calls are expected to last from 10-15 minutes each.

Education Control
Participants assigned to this condition will be instructed to go about their usual activities and will receive education about PA and a healthy lifestyle for MBC patients. They will be encouraged to download the free Cancer.Net app which contains a Metastatic Breast Cancer Coach module. The Cancer.Net App content includes information about health and well-being, treatment guidelines specific to their cancer type medication and symptom tracking, a spot to save questions for future appointments and an appointment calendar.

At the end of the 12 week intervention, participants in the education control group will receive a Fitbit and have access to the *Fit2ThriveMB* study app. If they choose to download the app and use it, the app will collect data including: login frequency, app usage, data entered into the app including symptom burden, goal selection and physical activity and data transmitted from the Fitbit, including physical activity and steps taken. This data will be collected for 12 months and stored for the purpose of analyzing post-intervention app usage and physical activity patterns. At the end of 12 months the app will no longer function. Participants will be instructed in how to download, and provided with written instructions for removing the app, if they wish following the 12 week assessment. Once the app is removed we will be unable to collect any data from their phone.

Support Calls
To match *Fit2ThriveMB* contacts, participants will also receive weekly calls that will cover health and well-being topics (see Table 3). They will be provided with the Fitbit after completion of week 12 assessments.

Table 3: Healthy Living Control Coaching Call Content

Week	Theme
1	Mindfulness
2	Social Support: Friends, Family, Counseling and Support Groups
3	Social Support: Online Communities
4	Symptom Tracking

5	Art Therapy/Doing Activities you Enjoy (focus on quality of life
6	Sleep
7	Fatigue
8	Cognition
9	Hydration
10	Nutrition
11	Healthy Grocery Shopping
12	Stress Management

Study Retention Plan

To minimize attrition, study staff will develop good rapport with participants during recruitment and maintain the relationship throughout the study (e.g., by sending birthday cards). Participants will be provided with a phone number to call immediately if they encounter issues with any aspect of the intervention. Staff will convey reminders of scheduled assessments by phone, email, or text message, per participant preference. Participants will also be incentivized to complete assessments ($41.50 at baseline and 12 weeks) for a total of $83.00. Participants will be paid $40.00 for completing the assessments in their entirety, and will be paid an additional $1.50 at each time point to cover the cost of transferring the electronic payment to a personal checking account, if the participant chooses. Also, participants will receive a free Fitbit.

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

If a participant in the intervention group does not track any activity via the Fitbit for 7 consecutive days and does not respond to any other study-related requests, study staff will reach out to the participant via phone and/or e-mail so they can be contacted for troubleshooting and engagement support. Participants will also identify two friends or relatives that can be notified if contact with the study participant fails to respond to our contact attempts. If we are unable to reach a participant after 3 phone calls or emails and a final email attempt, or they do not start recording data again after 2 weeks, we will contact the participant's emergency/locator contacts. For control participants, we will contact emergency/locator contacts if the individual does not respond to two weekly telephone calls (with 3 phone call attempts each) and a final email attempt. Participants will identify two emergency/locator contacts that may be notified if contact with the study participant is lost. Emergency/locator contacts will be associates of the participant who have a different telephone and email address from the participant and who agree to serve as emergency contacts for the participant. One locator/emergency contact must not live in the same house as the participant. We will only attempt to contact an emergency/locator contact if we are unable to reach a participant according to the rules outlined above or in the event of an emergency. We will only make one phone call attempt to reach an emergency/locator contact. If we are unable to reach the contact, we will attempt to leave a voice mail and follow-up with an email with the participant copied.

Measures

Table 4 displays a timetable for all assessments that occur at a discrete time point.

Primary Outcome: Feasibility and Acceptability

Feasibility

Feasibility will primarily be assessed via: a) participant retention (# of participants who drop out/ # randomized) and b) intervention adherence (% days adhere to daily goal and % of days wear Fitbit). The Fitbit is sufficiently well-validated for steps to support its role as an adherence measure in this study.

Adherence
Adherence during the 12 week intervention will be monitored continuously using Fit2ThriveMB app. As in our ongoing Fit2Thrive trial, we will obtain tracker wear time, steps, and time spent in sedentary, light, moderate, and vigorous intensity activity. Acceptability will be measured via a process evaluation of perceptions of MBC patients' experiences with Fit2ThriveMB.

Secondary Outcomes

Physical Activity and Sedentary Behavior

Actigraph Accelerometer**:** The ActiGraph accelerometer (model wGT3X- BT, ActiGraph, Pensecola, FL), a well-validated and reliable measure of objective PA[22, 23] will be used. It is blinded to the participant (i.e., no display or feedback). At each time point, participants will wear the device for 7 consecutive days during all waking hours, except when bathing or swimming. Participants will be instructed on how to wear the device and will use a log to record wear time and note any deviations from the wear protocol. After each wear period, data will be downloaded and screened for completeness and irregularities. Participants will be asked to re-wear the ActiGraph if it was not worn for at least 10 hrs/day for ≥5 days. Sixty consecutive zeros will be designated as non-wear time. Data will be collected in one-minute intervals (epochs). Each valid minute of wear time will be classified according to intensity (counts/min) using commonly accepted cut-points: sedentary (<100), light activity (100-2019) and MVPA (≥2020).[24, 25]

Sitting Time Questionnaire.[26] Women will be asked to indicate the amount of time they spend on a typical weekday and weekend sitting in the following activities: traveling to and from places, while at work, while watching television, while using a computer at home in leisure time NOT including television (e.g. visiting friends, movies, dining out, etc.). Test-retest reliability coefficients were high for weekday sitting time at work, watching television and using a computer at home (r_s=0.78-0.84) but are more variable for weekend days across all domains (r_s=0.23-0.74).

Godin Leisure Time Exercise Questionnaire (GLTEQ).[27] The GLTEQ is a simple, self-administered instrument that has been widely used in epidemiological, clinical, and behavioral change studies and has been shown to be both a valid and reliable measure of PA participation. Participants will be asked indicate the frequency and average amount of time they spent engaging in strenuous (e.g., jogging), moderate (e.g., fast walking), and mild (e.g., easy walking) exercise over the past seven days. Weekly frequencies of strenuous, moderate, and light activities are multiplied by nine, five, and three, respectively. These values are added to obtain a total leisure activity score. Test-retest reliability coefficient range from r=0.48 for light and moderate activity to 0.94 for strenuous. For total values the test-retest reliability coefficient is 0.74.[27] **Breast cancer survivors will also answer a modified version asking them about their PA *before diagnosis* at baseline.**

Symptom Burden and QOL

PROMIS Fatigue Short Form 8a.[28] The PROMIS Fatigue Short Form 8a will be used to assess participants' frequency of fatigue symptoms ranging from 1 (not at all) to 5 (very much) and fatigue interference ranging from 1 (never) to 5 (always) over the past 7 days. Higher scores reflect higher levels of fatigue. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

PROMIS Depression Short Form 8a.[28] Participants are asked to indicate the frequency of a variety of depressive symptoms over the past 7 days on a 5 point scale from 1 (never) to 5 (always). Higher scores reflect higher depressive symptoms. The reliability of this measures ranges from α=0.90 to α=0.95.[29]

PROMIS Anxiety Short Form 8a.[30] This measure assesses self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). Participants indicate how frequently they felt each anxiety symptom over the past 7 days on a scale from 1 (never) to 5 (always). Higher scores reflect higher more anxiety symptoms. The reliability of this measures ranges from α=0.90
to α=0.95.

PROMIS Emotional Support Short Form 8a. This measure assesses perceived feelings of being cared for and valued as a person; having confidant relationships. Participants indicate on a scale from 1 (never) to 5 (always) how often they feel they have emotional support when needed. Higher scores indicate greater emotional support.

PROMIS Pain Interference Short Form 8a.[30] This measure assesses the self-reported consequences of pain on relevant aspects of one's life. This includes the extent to which pain hinders engagement with social, cognitive, emotional, physical, and recreational activities. Participants how much pain had interfered with different aspects of their life on scale from 1 (not at all) to 5 (very much). Higher scores reflect greater pain interference. The reliability of this measures ranges from α=0.90 to α=0.95.36

PROMIS Physical Function Short Form 20a.[28] The PROMIS Physical Function Short Form 20a will be used to assess participants' physical function. The scale has two subscale limitations and interference. For the 6 limitations items, participants will rate the level of difficulty they have had executing discrete activities over the past 7 days on a scale from 1 (unable to do) to 5 (without any difficulty). For the 4 limitations items, patients will rate the degree to which their health limits them in specific activities on a scale from 1 (cannot do) to 5 (not at all). Higher scores reflect better physical function. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

Functional Assessment of Cancer Therapy-Breast[30] The 27-item Functional Assessment of Cancer Therapy-Breast (FACT-B)[37] will assess participants' physical, social/family, emotional and functional well-being as well as breast cancer specific concerns. Participants will be asked to indicate how true each of the items had been for them over the last 7 days on a five-point Likert-scale ranging from 0 (not at all true) to 4 (very much true). The total score is obtained by summing all of the items and then dividing by the number of items answered. Well-being subscale scores are calculated by multiplying the sum of the items from each subscale by the number of items in the subscale and then dividing by the number of items answered. Higher scores reflect better QOL. The internal consistency for the total score is high (α=0.90). Subscale alpha coefficients range from 0.63 to 0.86.

PROMIS Applied Cognition-General Concerns Short Form 8a.[28] The PROMIS Applied Cognition General Concerns Short Form 8a will be used to assess participants' frequency of perceived cognitive function over the past 7 days ranging from 1 (not at all) to 5 (very often). Higher scores reflect higher levels of cognitive concerns. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

PROMIS Applied Cognition-Abilities Short Form 8a.[28] The PROMIS Applied Cognition Abilities Short Form 8a will be used to assess participants' functional abilities with regard to cognitive tasks including the perception that one's cognitive ability with regard to the domain of inquiry (e.g. concentration, memory) has not changed. Participants will indicate their responses on perceptions of change over the past 7 days on a scale from 1 (not at all) to 5 (very often). Higher scores reflect higher levels of cognitive concerns. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

PROMIS Sleep-Related Impairment Short Form 8a. [28] The PROMIS Sleep –Related Impairment Disturbance Short Form 8a will be used to assess participants' perceptions or sleep-related impairment on a scale ranging from 1 (not at all) to 5 (very much). Higher scores reflect higher levels of sleep-related impairment. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

PROMIS Sleep Disturbance Short Form 8a.[28] The PROMIS Sleep Disturbance Short Form 8a will be used to assess participants' rating of overall sleep quality from 1 (very good) to 5 (very poor) and perceptions of specific characteristics of sleep quality on a scale ranging from 1 (not at all) to 5 (very much). Higher scores reflect higher levels of sleep disturbance. The reliability of this measure ranges from α=0.90 to α=0.95.[29]

Functional Performance

Short Physical Performance Battery (SPPB). Participants will also complete the Short Physical Performance Battery (SPPB), a well-validated physical function performance measure.[31-33] The SPPB score is based on timed measures of gait speed, ability to rise from a chair, and standing balance. Gait speed will be measured using the better of two recorded times over a 4-meter course. Chair stand time will be measured as the time needed to rise five times from a seated position in a chair, with arms folded across the chest. For the balance test, participants will be asked to maintain their feet side-by-side, semi-tandem, and tandem positions for 10 seconds each. Each individual performance measure will be scored according to established cutpoints[31, 33] and aggregated for a total SPPB score.

Senior Fitness Test.[34] We will use several items from the Senior Fitness Test including a) the 8-Foot Up-and-Go, a test of physical agility and dynamic balance, which measures the speed at which an individual walks around a cone or other object 8 feet away and back; b) the Arm Curl test, which assesses arm muscle strength endurance, specifically of the biceps, by measuring the number of arm curls that can be completed using a 5 lb weight in 30 seconds; c) and the 2 Minute Step Test, an aerobic endurance test, which counts the number of full in-place steps completed in two minutes. Participants will also complete a 30- second one leg stand test on each side (right and left) where they are instructed to stand on one foot for up to 30 seconds and timed.

6 minute walk.[35] MBC patients will complete a 6 minute walk test to assess their submaximal level of functional capacity. The goal is for the participant to walk as far and she can during these 6 minutes. Distance is measured once the 6 minute walk is complete, and provides information regarding cardiopulmonary and musculoskeletal systems that are used during physical activity that points toward exercise tolerance. Participants will be instructed to wear the accelerometer and a pedometer for the duration of the 6 minute walk test and will be instructed in the use of the provided blood pressure monitor and heart rate monitor.

Additional Exploratory or Confounding Variables

Demographics/Health History. Participants will self-report demographic information (i.e. age, race) and health history.

Medical Record Data. Medical record data will be obtained on clinical factors (date of diagnosis, treatment received, medication, comorbid conditions).

Body weight and height. Weight and height will be self-reported by participants. Weight will be measured on the subset of participants who own a digital scale, to the nearest 0.1 lb.

COVID-19 Assessment Questions. Participants will answer questions regarding the impact the COVID-19 pandemic has on physical activity habits, work, and their current living situation. These questions will only be asked of participants who participate in the study during the COVID-19 pandemic.

Social Cognitive Theory Constructs

Exercise Self-efficacy Scale.[32] The 6-item Exercise Self-Efficacy Scale will be used to assess participants' beliefs in their ability to exercise five times per week, at a moderate intensity, for 30 or more minutes per session at two week increments over the next 12 weeks. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). The internal consistency for this measure has demonstrated acceptability (α=0.90).[32]

Barriers Self-efficacy Scale.[32] The 15-item Barriers Self-Efficacy Scale will be used to assess participants' beliefs in their ability to exercise three times per week for the next 3 months in the face of commonly experiences barriers to activity. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). The internal consistency for this measure has demonstrated acceptability (α=0.86).[32]

Rosenberg Self Esteem Scale [36]. Global self-esteem was assessed via the Rosenberg Self-esteem scale. This scale has been widely used in several domains of self-esteem research including physical activity (Fox, 1997). This scale consists of 10-items asking participants to indicate their level of agreement/disagreement with each statement. Sample items include: "I feel that I'm a person of worth, at least on an equal basis with others;" and "I am able to things as well as most people." Participants respond on a 5-point Likert scale ranging from 1 (strongly agree) to 5 (strongly disagree). Responses are summed to yield a total score ranging from 10 to 50. Several researchers have demonstrated acceptable internal consistency and convergent validity (Curbow & Somerfield, 1991; Wylie, 1989).

Physical Self-Perception Profile (PSPP)[37]. The PSPP is a 30-item instrument used to assess self-esteem relative to several domains of physical functioning in a hierarchical, multidimensional fashion. The instrument contains a general physical self-worth scale (PSW) which subsumes four more specific scales of perceived sport competence (SPORT), physical condition (COND), attractive body (BODY), and strength (STRENGTH), with six items per scale. Participants indicated on a four-point scale the degree to which each item is characteristic or true of them. Responses range from 1 (not at all true) to 4 (completely true). [38]

Multidimensional Outcome Expectations for Exercise Scale.[33] This scale will assess participants' social (4 items), self-evaluative (5 items), and physical (6 items) outcome expectations for exercise participation as well as cancer specific outcomes (4 items) on a 5 point scale ranging from 1 (strongly disagree) to 5 (strongly agree). The three subscales have demonstrated good internal consistency (α= 0.82 for physical outcome expectations, α= 0.81 for social outcome expectations, and α= 0.84 for self-evaluative outcome expectations).[33]

Exercise Goal-setting Scale.[34] This 10-item scale will assess participants exercise-related goal-setting, self-monitoring and problem solving and instructs participants to indicate the extent to which each of the statements describes them on a scale from 1 (does not describe) to 6 (describes completely). This scale has demonstrated good internal consistency (α= 0.89). [34]

Social Support for Exercise Scale.[36]This scale assesses the degree to which friends and family have demonstrated support for exercise behaviors in the previous 3 months. The frequency for each item is rated once for both family and friends on a 5-point Likert scale, ranging from 1 (never) to 5 (very often). The friend and family subscales have demonstrated acceptable internal consistency (α=0.84 and α=0.84, respectively). [38]

Physical Activity Enjoyment Scale.[37] This 18-item scale will assess the degree to which participants, at the current moment, enjoy doing any sort of physical activity. This 18-item scale rates enjoyment on a 7-point bipolar scale ("It makes me depressed"…"It makes me happy"). This measure has demonstrated good internal consistency in previous studies (α= 0.93 to α= 0.96).[39]

Lifestyle Self-Efficacy 10,000 Steps. This 6-item scale assesses participants' beliefs in their ability to accumulate 10,000 steps per day for most days at two week increments over the next 12 weeks. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). This measure was added as part of modification 13 so will only be asked at baseline and week 3 for those participants who begin the intervention after approval of that modification.

Self-Efficacy of Walking Number of Steps. This 10-item scale assesses participants' beliefs in their ability to accumulate a step value in a day at 1,000 step increments starting at 3,000 steps until 12,000 steps. Items will be rated on a 100-point percentage scale with 10-point increments, ranging from 0% (not at all confident) to 100% (highly confident). This measure was added as part of modification 13 so will only be asked at baseline and week 3 for those participants who begin the intervention after approval of that modification.

Fidelity

Fidelity will be examined via the following metrics: % of days reported symptom burden; % of days set personalized goal; % of coaching calls attended, % of days posted on message board; % of app notifications read.

Table 4. Measures Time Table

Measure	**w0**	**w3**	**w12**
PAR-Q	X		
FRQ	X		
Demographics	X		
Health History	X		X
Physical Activity History	X		
Barriers Self Efficacy (BARSE)	X	X	X
Rosenberg Self Esteem Scale	X		X
Physical Self-Perception Profile (PSPP)	X		X
Exercise Goals Setting Scale (EGSS)	X	X	X
Exercise Self-Efficacy Scale (EXSE)	X	X	X
FACT-B	X		X
Godin GLTEQ_Current	X		X
Godin GLTEQ_Before Cancer	X		
Lifestyle Self-Efficacy 10,000 Steps	X	X	X
MOEES	X	X	X
Physical Activity Enjoyment (PACES)	X	X	X
PROMIS Applied Cog. General Concerns	X		X
PROMIS Anxiety 8a	X		X
PROMIS Depression 8a	X		X

PROMIS Fatigue 8a	X		X
PROMIS Emotional Support	X		X
PROMIS Pain Interference 8a	X		X
PROMIS Phys. Function 20a	X		X
PROMIS Sleep Disturbance 8a	X		X
PROMIS Sleep-related Impairment 8a	X		X
PROMIS Applied Cognition	X		X
Self-Efficacy of Walking Number of Steps	X	X	X
Social Support Exercise (SSE)	X	X	X
Sitting Time Questionnaire (STQ)	X	X	X
Process Evaluation			X
COVID-19 Assessment	X	X	X
Weight	X		X
Blood Pressure	X		X
SPPB	X		X
Senior Fitness Test	X		X
6 minute Walk	X		X

Data quality control/checking

The majority of data is collected (PA, symptoms, acceptability) or uploaded electronically. The quality of these data will be checked by examining descriptive statistics and score ranges of all variables for missing and/or erroneous values. All data will be examined for violation of basic statistical assumptions (i.e. normality, multicollinearity) and transformed, if needed. Participants will be asked to complete all assessments, regardless of group assignment or adherence. Strategies for handling missing data (i.e. maximum likelihood estimation, multiple imputation) will be chosen based on the type and extent of the problem.

Statistical Analyses Plan

Aim 1. Feasibility and acceptability will be analyzed using descriptive statistics (frequencies, means and standard deviations). Feasibility will primarily be evaluated using the "successful completion rate" defined as: a) ≥80% of MBC patients who enroll in the intervention will remain in the intervention and b) MBC patients will adhere to daily goals and wear Fitbit ≥70% of study days (i.e. ~59/84 days) If a successful completion rate is achieved, *Fit2ThriveMB* will be deemed feasible. Additional measures of feasibility, fidelity, acceptability and safety will also be summarized and considered with the "successful completion" rate before proceeding with a more definitive trial.

Aim 2 and Exploratory Aim. We will employ an intent-to-treat (ITT) approach by including all participants recruited into the study regardless of compliance. Every effort will be made to collect all outcome measures even if a participant does not engage in assigned treatments. Analysis of covariance (ANCOVA) will be used to compare study groups with respect to mean changes in each outcome from baseline to 12 weeks with baseline adjustment. Data from these analyses will provide estimated means, standard errors, and preliminary effect sizes for the *Fit2ThriveMB* intervention. These data will be used for future sample size calculations, to identify a primary endpoint and further refine the *Fit2ThriveMB* intervention to be tested in a more definitive trial. We will also use regression models to explore the relationship between changes in each outcome and intervention adherence. This study is not designed to make conclusions about *Fit2ThriveMB* efficacy without further study.

Timeline
The overall duration of the study will be 2 years, and each participant will be actively participating for 12 weeks.

10.0 Research with Vulnerable Populations:

Non-English Speaking Subjects: N/A

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

Cognitively Impaired Adults: N/A

Adults Unable to Consent: N/A

11.0 Incomplete Disclosure or Deception: N/A

12.0 Consent Process:

Consent will always be obtained before a subject participates in any component of the current protocol. Patients who are eligible after screening and express interest in the study will be scheduled for a recruitment phone call. Study staff will review details of the study and answer any questions. Patients who are still interested will be sent an email with a link to the online consent form housed in REDCap. All participants will complete an online version of the informed consent. Because we are asking participants to type their full name on any on-line consents, this is considered equivalent to a written signature. They will also be emailed a copy and instructed to print a copy or to contact the study team at any time if they would like a copy for their records. A telephone number and e-mail address for the PI will be provided on the informed consent page, in the event they should have any questions or need clarification. The informed consent will clearly state that participation in the present study is completely voluntary and participants can discontinue or withdraw at any point without penalty.

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

This study is covered by a certificate of confidentiality. Language describing the Certificate of Confidentiality will be included in the consent form.

13.0 Research with children: N/A

14.0 Waiver of Participant Signature on Consent Form:

This waiver is being requested as part of the screening process. Screening data collected prior to obtaining informed consent includes name, contact information, demographic information and basic medical and health information. Demographic information collected during the screening survey is used to help the study team understand relations between demographic information and study eligibility as well as who chooses to participate in the study. Basic medical and health information collected during the screening survey helps to

determine eligibility for the project. This information is obtained online or through a phone conversation after potential participants are given the research study details. Participants agree to provide this information online or verbally, and allow us to retain it even if they do not participate in the study, however, they are not required to sign the screening. Thus, a waiver of participant signature is required. These data are recorded in RedCap, a password-protected database, only accessible by the research team. The subject provides all data freely. Data for CONSORT purposes will be linked by subject ID, not by name, thus protecting the subject's privacy. Therefore, this aspect of the study contains little, if any, risk to the subject. This waiver is requested because determining subject eligibility is only possible by obtaining basic demographic and medical health history information during screening, and understanding the effects demographic information has on study eligibility and recruitment may help to strengthen future recruitment strategies Potential participants will be provided with reason(s) for ineligibility via our online survey (RedCap) or initial phone conversation. All subjects will be given the opportunity to be contacted regarding future research opportunities if they so choose, and their contact information will be kept in the database for this purpose. If they prefer no future contact, their name and contact information will be deleted from the database but the information they have previously provided will be used for final CONSORT purposes.

15.0 Waivers and Alterations of Consent Information: N/A

16.0 Financial Compensation:

Participants will be paid for completion of assessments ($41.50 at baseline and 12 weeks) for a total of $83.00. Participants will be paid $40.00 for completing the assessments in their entirety, and will be paid an additional $1.50 at each time point to cover the cost of transferring the electronic payment to a personal checking account, if the participant chooses. The payment will be sent as an e-giftcard that participants will receive in their email. If participants only complete a portion of the assessment at either time point or withdraws before completing any portion of the assessment at either time point, payment will be pro-rated as follows: $10 for completing the questionnaires, $15 for wearing the accelerometer and $15 for completing functional performance testing.

All participants that complete baseline and 12 week testing will also be allowed to keep their Fitbit (intervention group) or be given a Fitbit (control group).

17.0 Audio/Video Recording:

All participant coaching calls (intervention group) and weekly calls (control group) will be digitally audio recorded for quality control and training purposes for those participants who agree. All participant remote functional performance video conference testing will also be recorded for research, training and quality control purposes. Digital files will be stored on a password-secured network drive that is only accessible by the study team. Only participants' first names will be used during any recorded sessions. Recordings may be transcribed verbatim and de-identified. Recordings will be destroyed at the end of the study. All subjects will have the option to withdraw from recordings at any time for any reason.

Participants who agree may be photographed or video recorded during Zoom video conferences.Participants may also post photographs or videos of themselves on the study application message board. Photographs or videos we obtain either way may be used for scholarly presentations or publications if a participant agrees.

18.0 Potential Benefits to Participants:

The benefits of physical activity are well established. Intervention participants may experience significant decreases in symptom burden and improved physical and psychological functioning and quality of life. If the proposed *Fit2ThriveMB* intervention proves to be feasible, acceptable and shows promise for efficacy it could have high scalability potential and be applicable to other advanced cancer populations or other populations with

chronic disease. Additionally, this study will produce societal benefit regarding new knowledge about how technology-supported physical activity interventions can effectively change behavior in metastatic breast cancer patients.

Given the minimal risk of study participation and potential benefits, we believe the risks to subjects are reasonable in relation to the anticipated benefits to research participants and others.

19.0 Risks to Participants:

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

There is also the small chance a participant could strain, fall or injure themselves during the functional performance video conference. However, again, serious physical injury is considered unlikely. In order to reduce and/or prevent injuries during testing, two study staff members will be present on the video conference to provide remote assistance. Study staff will be thoroughly trained on assessment procedures and be required to follow specific scripts to ensure safety. Further, all staff who participate in testing will be required to be First-Aid/CPR/AED certified and will be available to provide verbal instructions to a participant or a participant's support person if needed in the unlikely event of an emergency situation. Staff will be required to use a computer for the functional performance video conference, and keep their cell phone available in the event of an emergency. Study staff will take measures to ensure participants will be able to receive timely medical assistance in the unlikely event of an emergency. At the beginning of each functional performance video conference session, study staff will confirm and record the address of the residency that the participant is completing testing, the participant's phone number, whether there is someone at home with the participant, the closest cross streets to the residency and whether there is a support person in the house. Further, if there is someone at home with the participant, we will ask for, record his or her name, and ask if this person is available within shouting distance if needed. Study staff will be prepared to use this information to call the participant's local non-emergency phone number, if necessary, to be directed to their local emergency dispatch team to ensure that medical help will arrive as quickly as possible. In addition, participants will be instructed to keep a telephone close by and a sturdy chair close by to aid in balance. Finally, if possible, participants will be asked to have a support person present in the house during the video conference session and have that person within shouting distance for the duration of the test.

In addition to the potential minimal risk associated with PA participation and remote functional performance testing, there are some potential minimal psychological risks associated with answering some of the questionnaires required for participation in this study. However, participants will be given the option to skip any questions that make them feel uncomfortable. Should any individuals report scores on the PROMIS Cancer Depression Scale, that are in the 75th percentile (i.e. ≥ 4.3) or confer a high level of distress in interactions with research study staff, they will be referred to the Supportive Oncology program at Northwestern: https://www.cancer.northwestern.edu/cancer-care/patient-support/index.html.

There may also be a security risk in using Zoom video conference software to communicate with participants during remote functional performance testing and orientation sessions. In order to minimize the risk of using Zoom video conference software and enhance security, all participants will be sent individual links to attend the

video conference to their email with a password that will be required to enter the meeting. Study staff will also enable the 'waiting room' feature on Zoom so that only members permitted by the meeting host (study staff member) will present in the video conference.

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

Participants are permitted to refuse to participate in any aspect of the research and may withdraw from the study at any point, for any reason without penalty. For any participant who elects to withdraw, permission will be sought to continue to collect outcome data for use in the analysis. However, all participants in the intervention will be accounted for in all follow-up analyses following the intent-to-treat principle. If participants withdraw from the study, and do not agree to return for follow-up assessments, data from their most recent assessment will be carried forward and imputed in subsequent assessment points (Last Observation Carried Forward).

Protection against Risk

The following procedures will be used to minimize risk:

- Numerous studies have demonstrated that physical activity is safe, feasible, and beneficial for cancer patients and survivors, including those with advanced disease.
- Potential participants will be screened using a standard tool to assess readiness to engage in physical activity.
- All participants will be required to obtain medical clearance from their oncologist. This ensures that we will enroll only those patients whose clinicians approve for the study.
- Our study physician, Dr. Gradishar, will be available to assist with medical questions that may arise during screening or the intervention itself. If the study physician has any concerns, participants will be referred to their own physician for consultation.
- Participants will be instructed to increase physical activity gradually and tailored to their own abilities.
- Participants will receive tips to help prevent soreness and injury.
- Participants will be asked to contact the study coordinator at any time if they have questions or concerns about increasing their physical activity level.
- All study files, folders, and records will be kept in locked file cabinets that can be accessed only by study personnel.
- All data will be exchanged over an SSL-protected connection, and all data will be encrypted prior to storage using an encryption key known only to the investigators. No PHI will be included in the *Fit2ThriveMB* app.
- The study database and all survey data will be collected and stored in REDCap, which has the protections needed for storage of PHI.

20.0 Provisions to Protect the Privacy and Confidentiality of Participants and the Research Data:

Participant databases and survey responses

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

To ensure the integrity of the data collected from study participants several procedures will be implemented. All personnel involved in data collection will be thoroughly trained in all assessment methods thus ensuring consistent applications of procedures and measurement consistency across participants. All questionnaire assessment data will be automatically saved in the secured, password protected REDCap system and will be downloaded to a password protected network folder protected ensuring access only by the investigators. Any hard copies of data will only include the participants ID number and will be entered into the REDCap system only using this ID number and will be stored in a separate, locked cabinet from the informed consents in the PI's laboratory.

Files containing identifying information obtained for purposes of tracking participants and monitoring of subject payments are kept in a locked file in a locked office separate from study related data. Data will only be linked to identifying information through a study ID. Under no circumstances will individually identifiable data be released to anyone without the written consent of the subject. Results will be reported as group findings only. In the past we have found that all of these procedures are effective at reducing risk for study participants.

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

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

Fit2thriveMB app data

The Fit2Thrive mobile application was developed at Northwestern and is hosted by Northwestern. Participants will download the app to their own personal device. Data collected from the app is associated with an ID number not participants name or other identifying information. All data will be exchanged over an SSL-protected connection, and all data will be encrypted prior to storage using an encryption key known only to the investigators. All data are encoded during transfer between devices and the web server and prior to storage on the webserver. These data will reside on a secure, password protected server. Accordingly, these data are inaccessible to any person aside from the investigative team. These data are backed up regularly and are available for download only to the study investigators and must be accessed with a unique identifier and password combination.

All data will be kept for 7 years after publication, as required by Northwestern University.

Zoom Video Conference Software

Participants will participate in scheduled video conferences via Zoom at baseline and the 12 week assessment. Zoom video conferences will be recorded for research, quality control and training purposes, if the participant consents. Zoom recordings will be saved on a password-protected network folder. In order to protect patient safety and privacy during the Zoom video conference, each participant will receive an individual, secure link to join the meeting. All video conferences will require a password to enter, and we will enable the waiting room feature on all meetings so that the meeting host (study staff member) has to approve entry to every user that requests to enter the meeting.

21.0 Data Monitoring Plan to Ensure the Safety of Participants:

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

Events may also be spontaneously reported to staff during contact time. Adverse events and serious adverse events may also be identified during regularly scheduled calls or emails by researchers blinded to the treatment condition of the participant. These phone interviews or emails will be conducted every 4 weeks throughout the

12 week study period. Participants will be asked to complete the Non-spontaneous Adverse Events Questionnaire either via REDCap or via an interview with study staff. This form will be completed for all metastatic breast cancer survivor participants and will query the participant as to whether they have had any health and/or medical problems during the preceding 4 week period. Participants will be called or emailed until a response is received. Participants will also be required to provide the investigators with at least one emergency contact to have on file in the event we are fail to reach the participant after 5 or more attempts. If participant reports "YES" to item 5A-5D (see REDCap form), an adverse event form will be filed with the IRB.

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

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

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

22.0 Long-term Data and Specimen Storage and Banking:

All data will be kept for 7 years after publication, as required by Northwestern University. Questionnaire and accelerometer data will be stored electronically on a password network only accessible by study investigators. All hard copies of functional performance testing sheets will be stored in a secure, locked cabinet only accessible by study investigators and will also be manually entered into a REDCap database. The hard copies will also be scanned and uploaded to the password network. All data will be stored de-identified with study ID number only.

23.0 Qualifications to Conduct Research and Resources Available:

All staff (project coordinator, research assistants, interns) who are part of this study will complete Northwestern University requirements for the responsible conduct of research including the Collaborative Institutional Training Initiative (CITI) Training Modules. They will also undergo extensive training on research methods and study procedures.

The PI (Dr. Phillips) is an Associate Professor in the Department of Preventive Medicine and has a PhD in Kinesiology from the University of Illinois Urbana Champaign, MPH in Quantitative Methods from Harvard University and completed a postdoc at the National Cancer Institute. She has extensive training in randomized physical activity intervention in cancer survivors and older adults and has successfully conducted several other, similar, studies while at the University of Illinois Urbana Champaign.

Co-Investigators. Dr. Bonnie J. Spring, PhD is the Director of The Center for Behavior and Health and Professor in Preventive Medicine, and Co-Leader of the Cancer Prevention Program at RHLCC at NU. Dr. Spring has extensive experience in mHealth, behavioral intervention trials and MOST methodology. Dr. Julia Lee, PhD is an Associate Professor in Biostatistics and Preventive Medicine and an expert in using cutting-edge statistical techniques to analyze behavioral interventions and accelerometer data. Dr. Gradishar is the Betsy Bramsen Professor of Breast Oncology in the Department of Hematology and Oncology with expertise in breast cancer management and precision medicine clinical trials.

24.0 Data Sharing:

Data collected in this study will be made available to other researchers in compliance with the NIH Data Sharing Policy. We welcome inquiries by investigators who are not associated with the study to review or analyze data that we have collected. All requests for data sharing will be handled by the PI, Dr. Phillips, in conjunction with co-investigators, on a case by case basis to ensure that the proposed work does not conflict with planned analyses; we will also establish that the proposed project has sufficient scientific merit before proceeding. If a request is approved, we will develop data sharing agreements with outside investigators to safeguard the confidentiality of the data collected in our study in compliance with the NIH Data Sharing Policy. Before releasing data, we will reach an agreement with outside investigators regarding the need for scientific involvement on the part of the PI or other members of the research team. Before making the data available to researchers not involved in the proposed study, we will ensure that the data to be shared are de-identified and comply with both IRB regulations and the Privacy Rule under HIPAA regulations. Under no circumstances will personal identifying information, such as name, address, or telephone be shared with anyone outside our research team.

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