A BCT Intervention for Physical Activity Among Individuals on Statins
NCT05273723
PI: Karina Davidson, PhD, MASc
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RESEARCH PROTOCOL

Protocol Title:	The Effect of a Multi-Component Behavior Change Technique Intervention on Physical Activity Among Individuals on Primary Prevention Statin Therapy: A Dose-Finding Pilot Study
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Guidelines for Preparing a Research Protocol

Instructions:

- You do not need to complete this document if you are submitting an *Application for Exemption* or *Application for a Chart Review*.
- Do not use this template if:
  - Your study involves an FDA regulated product. In this case, use the *Clinical Trial Protocol Template.*
  - Your study has a protocol from a sponsor or cooperative group. In this case, use the *Protocol Plus*.
  - Your study is a registry or repository for data and/or samples, In this case, use *Protocol Template – Registry Studies.*
- If a section of this protocol is not applicable, please indicate such.
- Do not delete any of the text contained within this document.
- Please make sure to keep an electronic copy of this document. You will need to use it, if you make modifications in the future.
- Start by entering study information into the table above, according to these rules:
  - Protocol Title: Include the full protocol title as listed on the application.
  - Investigator: include the principal investigator's name as listed on the application form
  - Date Revised: Indicate the date at which the protocol was last revised
  - IRB Number: Indicate the assigned IRB number, when known. At initial submission, this row will be left blank.
- Once the table information in entered, proceed to page 2 and complete the rest of the form.

â Continue to next page to begin entering information about this study â

1. PREVIOUS STUDY HISTORY

Has this study ever been reviewed and rejected/disapproved by another IRB prior to submission to this IRB?

☒ No ☐ Yes - if yes, please explain:

2. BRIEF SUMMARY OF RESEARCH

- *The summary should be written in **language intelligible to a moderately educated, non-scientific layperson**.*
- *It should contain a clear statement of the rationale and hypothesis of your study, a concise description of the methodology, with an emphasis on what will happen to the subjects, and a discussion of the results.*
- *This section should be ½ page*

The purpose of this project is to identify the minimum effective dose (MED) of a multi-component behavioral change intervention required to increase levels of physical activity (PA) among participants on primary prevention statin therapy who are at elevated risk for cardiovascular disease (CVD). The long-term goal is to prevent CVD. The current project will utilize a modified version of the time- to- event continual reassessment method method (TiTE-CRM) [1,2] , a state-of-the-art dose finding methodology, to determine the MED of a multi-component behavioral change technique (BCT) intervention required to increase PA by an average of 2,000 steps per day. The intervention will be comprised of 5 BCTs which have previously shown to be effective on increasing health behaviors: Goal Setting, Action Planning, Self-Monitoring, Feedback, and Prompts/Cues [3-6].

The sample will include individuals prescribed primary prevention statin therapy with self-reported low levels of physical activity. Participants will complete a 2-week baseline run-in period where PA levels will be measured using Fitbit wearable devices and levels of adherence to statin medications will be assessed using eCAP smart pill bottles. During the baseline period, data from the Fitbit wearable devices will be used to verify participant's level of objective sedentary behavior. Individuals who are non-adherent to the protocol will be excluded and will not be randomized to the intervention. Following baseline, we will randomize 42 participants into 14 cohorts of 3 participants each for the intervention period. During the intervention period, participants will receive a BCT intervention, the length of which varies between 1 and 10 weeks depending on the assigned dose of a multi-BCT intervention. Assignment to doses will utilize modified TiTE-CRM methodology to adjust the dose for each cohort based on the results from the previous cohort. Following the intervention, all participants will be assessed over a 2-week follow-up period which includes passive data collection from the activity monitor, answering surveys and use of eCAP smart pill bottles to track medication adherence.

All collected data will be stored in the REDCap program, which is a Northwell IRB and Research IT security approved application, housed on the Northwell IT approved server. The MED will be defined as the smallest BCT dose duration associated with 80% of participants having a successful PA increase between the run-in and the follow-up periods. Change in PA will be defined as the difference in average daily PA between the run-in and follow-up periods. We will also assess Mechanisms of Action (MoAs) to determine potential mediators of the BCT intervention on PA. As increasing

PA may change statin adherence [7, 8], we will utilize eCAP smart pill bottles to measure adherence to statin medications.

3. INTRODUCTION/BACKGROUND MATERIAL/PRELIMINARY STUDIES AND SIGNIFICANCE

- *Describe and provide the results of previous work by yourself or others, including animal studies, laboratory studies, pilot studies, pre-clinical and/or clinical studies involving the compound or device to be studied.*
- *Include information as to why you are conducting the study and how the study differs from what has been previously researched, including what the knowledge gaps are.*
- *Describe the importance of the knowledge expected to result*

Cardiovascular disease (CVD) remains the leading cause of mortality [9] and morbidity [10]in the United States. Statin therapy is a mainstay of CVD prevention, with multiple, large randomized controlled trials (RCTs) demonstrating that statin therapy decreases the probability of CVD events [11-13]. . However, research has shown that statin therapy alone is insufficient for preventing incident CVD and mortality [8-11][14-16].

Walking an additional 2,000 steps per day has been found to have a clinically significant impact on CVD risk [16]. Combining statin medication with physical activity (PA) can lower mortality risk more than either statin or PA alone[14,15]. Further, the addition of PA to statin therapy can have additional benefits, such as increased cognitive functioning [17] and reduced side effects for statin therapy [18.19]. Despite the importance of increasing PA while on statins, PA levels often remain the same following statin prescription [20] and may even decline [21].

Multi-component behavioral change technique (BCT) interventions have demonstrated modest efficacy for increasing PA [22-24] and medication adherence [3,25]. However, no research has examined the dose of a multi-BCT intervention required to produce a clinically meaningful increase in PA. By using a modified version of the time-to-event continual reassessment method (TiTE-CRM), the current study can identify the required dose of a BCT intervention to increase PA by an average of 2,000 steps per day among individuals on primary prevention statin therapy at elevated risk for CVD.

4. OBJECTIVE(S)/SPECIFIC AIMS AND HYPOTHESES

- *A concise statement of the goal(s) of the current study.*
- *The rationale for and specific objectives of the study.*
- *The goals and the hypothesis to be tested should be stated.*

The current study aims to identify the required dose of a behavioral change technique (BCT) intervention to increase physical activity (PA) by an average of 2,000 steps per day among individuals on primary prevention statin therapy with elevated risk for cardiovascular disease (CVD). The study will utilize the modified time-to-event continual reassessment method (TiTE-CRM).

Primary Aim: Identify the MED of a multi-BCT intervention required to increase PA by an average of 2,000 steps per day between run-in and follow-up periods in at least 80% of participants.
Secondary Aim 1: To identify effect sizes for mediating MoAs of the BCT intervention on PA.
Secondary Aim 2: Identify additional benefits of the BCT intervention on statin adherence.
Exploratory Aim: Identify between-person heterogeneity in Treatment Response.

5. RESOURCES AVAILABLE TO CONDUCT THE HUMAN RESEARCH

- *Explain the feasibility of meeting recruitment goals of this project and demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period*
    - *How many potential subjects do you have access to?*
- *Describe your process to ensure that all persons assisting with the trial are adequately informed about the protocol and their trial related duties and functions*

Northwell Health employs over 77,000 individuals. Inter-departmental support has been shown across Northwell to assist the researchers in meeting recruitment goals. Their extensive electronic communication system will allow for the rapid delivery of recruitment materials directly to potentially-eligible participants. Virtual electronic screening and consent processes, employment of participant smart phones for protocol reminders and notifications, and integration with existing Northwell Health policies will minimize burden to participate for those who are interested in the study.

Center for Personalized Health staff must meet certain eligibility criteria before assisting with this study. All staff members must be listed on the IRB and be up-to-date with trainings and attestations as required by the Northwell Health Human Research Protection Program. Additionally, staff will be required to participate in weekly meetings with the Principal Investigator and an additional weekly meeting with the Project Manager, in order to stay informed about the study protocol, staff duties and functions, and to answer any questions that come up within the group. Staff will have daily access to the Project Manager, Director of Clinical Research, and Principal Investigator to answer any protocol questions they may have outside these established weekly meetings.

6. RECRUITMENT METHODS

- *Describe the source of potential subjects*
- *Describe the methods that will be used to identify potential subjects*
- *Describe any materials that will be used to recruit subjects. A copy of any advertisements (flyers, radio scripts, etc.) should be submitted along with the protocol.*
- *If monetary compensation is to be offered, this should be indicated in the protocol*

The study will be advertised to potential participants (those taking statin medication) via established Northwell communication channels, including email. This extensive electronic communication system allows for the rapid delivery of recruitment materials directly to potentially eligible participants including, but not

limited to, advertisement on TV monitors in office locations in collaboration with Northwell Marketing.

For additional recruitment, we will utilize the Quantitative Intelligence (QI) group to identify potential participants via history of statin medication prescription (to meet inclusion criteria) and diagnostic codes for cardiovascular disease and severe mental illness, via Touchworks. Potential participant's phone number and emails will also be collected. Once identified, eligible participants will be called directly and/or sent an email that provides a link to review the consent document if they are interested in participating or contact study personnel if they have questions. In situations where an individual is upset they have been contacted and/or the study team has their information for that purpose, we will clarify that no one on the study team has reviewed their records, but that we respect their privacy and they will not be contacted for this study again.

Recruitment links will lead to a study web page with more information about study requirements, eligibility, and who to contact for more information. There is no payment to subjects for participation in this research, however participants will be allowed to keep their commercially available Fitbit device at the end of the study . Participants will be required to return their eCAP smart pill bottle at the end of the research study.

7. ELIGIBILITY CRITERIA

- *Describe the characteristics of the subject population, including their anticipated number, age, ranges, sex, ethnic background, and health status. Identify the criteria for inclusion or exclusion of any subpopulation.*
- *Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners or other institutionalized individuals, or others who are likely to be vulnerable. You cannot include these populations in your research, unless you indicate such in the protocol*
- *Similarly, detail exclusionary criteria: age limits, special populations (minors, pregnant women, decisionally impaired), use of concomitant medications, subjects with other diseases, severity of illness, etc.*

Inclusion Criteria:

- Ages 18 or older;
- Ambulatory without limitations: has never been advised by a clinician that increasing low-intensity walking would be unsafe;
- Prescribed statin medication;
- Self-reported low levels of physical activity;
- Access to and capable of using a smart cellular phone;
- After 2-week run-in, objectively-verified low levels of physical activity as documented by a commercially available Fitbit device;
- English speaking.

Exclusion Criteria

- Age less than 18 years;
- Non-ambulatory or unsafe/not recommended to participate in a walking program;
- Not prescribed statin medication;
- History of CVD;
- Inability to comply with study protocol during 2 week run-in;
- Does not speak English;
- Unavailable for follow-up;
- Cognitive impairment;
- Severe mental illness (e.g., bipolar disorder or schizophrenia);
- Pregnancy

8. NUMBER OF SUBJECTS

- *Indicate the total number of subjects to be accrued locally. If applicable, distinguish between the number of subjects who are expected to be pre-screened, enrolled (consent obtained), randomized and complete the research procedures.*
- *If your study includes different cohorts, include the total number of subjects in each cohort.*
- *If this is multisite study, include total number of subjects across all sites.*

For this research, we will enroll up to 100 participants, with the goal of randomizing 42 individuals to the study intervention (14 cohorts of 3).

9. STUDY TIMELINES

- *Describe the duration of an individuals participation in the study*
- *Describe the duration anticipated to enroll all study subjects*
- *The estimated date of study completion*

Participants in this research could remain on study for up to 14 weeks.

All participants will undergo a 2 week run-in period and will then be enrolled in cohorts of 3. The first cohort will be given BCT intervention with a duration of 5 weeks. Subsequent cohorts will be given a BCT intervention duration (from 1-week to 10-week) based on the updated MED estimate according to the modified TiTE-CRM model and data from the previously enrolled participants. The process will continue until we reach a total of 42 participants (14 cohorts) randomized to the intervention; see sample size justification below.

All participants will then undergo 2 weeks of observation. In summary, participation will be between 5– 14 weeks depending on BCT dose assignment.

10. ENDPOINTS

- *Describe the primary and secondary study endpoints*
- *Describe any primary or secondary safety endpoints*

This study is a pilot whose primary purpose is to identify the MED of a multi-component BCT intervention needed to increase PA among participants on primary

prevention statin therapy. Secondary endpoints include pooling trial results across all participants to assess the mediation of MoAs for BCTs on physical activity and to identify any potential benefit of BCTs on increasing statin adherence.

11. RESEARCH PROCEDURES

- *Include a detailed description of all procedures to be performed on the research subject and the schedule for each procedure.*
- *Include any screening procedures for eligibility and/or baseline diagnostic tests*
- *Include procedures being performed to monitor subjects for safety or minimize risks*
- *Include information about drug washout periods*
- *If drugs or biologics are being administered provide information on dosing and route of administration*
- *Clearly indicate which procedures are only being conducted for research purposes.*
- *If any specimens will be used for this research, explain whether they are being collected specifically for research purposes.*
- *Describe any source records that will be used to collect data about subjects*
- *Indicate the data to be collected, including long term follow-up*

Potential participants will be first linked to an authorization form, allowing the study team to collect PHI necessary for the study. Participants who authorize PHI collection will then be asked to provide demographic information needed to comply with NIA reporting requirements. This basic demographic information (including age, sex, race, and ethnicity) will be used by the study sponsor for the purpose of determining equity and representativeness in recruitment for clinical trials. This demographic information is collected prior to eligibility screening to ensure that the study is not excluding potential participant groups. Afterwards, participants will be directed to an electronic screening questionnaire administered via REDCap to determine their eligibility. If eligible, participants will be automatically allowed to review and sign an informed consent form. Those who have signed the informed consent form are encouraged to discuss study procedures and address any questions with a clinical research coordinator. Prior to receiving study devices, participants will read and sign a device allocation document letting them know which devices they may keep upon study completion and which devices should be returned to study staff. Both eligible and ineligible participants will be presented with a series of optional demographic questions. Asking these questions is required by the study sponsor (NIA) with the intention of improving equity and representativeness in clinical trial recruitment. The optional questions are presented regardless of eligibility to ensure that the study is not excluding potential participant groups. These demographic questions will be provided to the NIA, the study sponsor, as part of the continuing report process. Study staff will set up the eCAP device and assign it to participants as they are enrolled and consented. Participants who sign consent will then be asked to answer some demographic questions during onboarding and will be mailed a commercially available Fitbit device and eCAP smart pill bottle after onboarding is complete. Upon receiving the smart pill bottle, participants will fill the eCAP pill bottle using their existing statin prescription.

The intervention will utilize the modified TiTE-CRM design as well as 5 BCTs, which

have previously been shown to be effective on increasing health behaviors: Goal Setting, Action Planning, Self-Monitoring, Feedback, and Prompts/Cues. *Goal setting* is setting a goal defined in terms of the behavior to be achieved. For example, an individual may set a goal to walk 6,000 steps per day. *Action planning* is detailing the plan of where, for how long, and at what time physical activity is going to be performed. This BCT involves encouraging one to decide to act or set a behavioral resolution by forming *detailed plans* that link the behavior to specific situational cues. For example, a participant can decide they will walk for 30 minutes on weekdays following breakfast. *Self-monitoring of behavior* is defined as monitoring and recording behavior. For example, a person can keep a record of when they walk and the number of steps walked. *Feedback on behavior* is defined as providing informative or evaluative feedback on the performance of the behavior. For example, a person may receive a text message informing them they walked 42,000 steps over the past week, an average of 6,000 steps per day. *Prompts/cues* is defined as introducing or defining environmental and social stimuli with the purpose of prompting or cueing behavior. For example, texting a patient 30 minutes prior to a scheduled time for walking is an example of this BCT.

Participants begin the trial with a 2-week run-in period during which their baseline levels of PA (assessed using a Fitbit device) and compliance with study protocol will be assessed. Participants will also complete one questionnaire at the end of their baseline period to assess MoAs.

Mechanisms of action (MoAs): This study will assess 5 potential MoAs by which BCTs may influence physical activity (walking) behavior. All MoA measures will be assessed bi-weekly (if applicable according to BCT package) via one electronic survey presented using RedCap

Beliefs about capabilities / self-efficacy for walking is defined as beliefs about one's ability to successfully perform a behavior. Beliefs about capabilities/self-efficacy will be assessed using the Self-Efficacy for Walking (SE-W) scale,[26] a 10-item measure assessing patient's capabilities to walk for durations of 5 to 50 minutes. Items are scored from 0 to 100%, with scores of 0% indicating participants are "not at all confident" they could walk for that duration and scores of 100% indicating the participants are "highly confident" they could walk that duration. Items are averaged to create a total score, with higher scores indicating higher levels of beliefs about capabilities/self-efficacy.

Behavioral regulation/ intrinsic regulation is defined as behavioral, cognitive, and/or emotional skills for managing or changing behavior. Behavioral regulation will be assessed using a 4-item measure assessing intrinsic regulation, a subscale of the Behavioral Regulations in Exercise Questionnaire Version 2 (BREQ-2) [27]. Items are scored on a 0 (Not true for me) to 4 (Very true for me) scale, and averaged to create a total score, with higher scores indicating greater behavioral regulation capability.

Feedback processes/discrepancy in behavior is defined as processes through which current behavior is compared against a particular standard. Feedback processes will be assessed with a single item measuring discrepancy in behavior adapted from

Curtin and colleagues [28]. The text of the measure is "How large is the difference between your current walking behavior and your goal concerning your walking?" The question is rated from 0 (Not at all different) to 7 (very different) with higher scores indicating greater levels of discrepancy in behavior.

Motivation is defined as processes relating to the impetus that gives purpose or direction to behavior, and operates at a conscious or unconscious level. Motivation will be assessed with a message stating "I feel motivated to walk each day." Participants will rate this item on a scale of 0 (Not true at all) to 7 (Very true) with higher scores indicating higher levels of motivation.

Environmental context and resources is defined as aspects of a person's situation or environment that discourage or encourage the behavior. This MoA will be assessed using a checklist of 7 potential barriers to physical activity identified by Steinhardt and colleagues [29] Barriers are coded on a 1 (Not often at all) to 5 (Very often) scale, and averaged to create a total score, with higher scores indicating that the listed barriers had greater effects on walking.

Following completion of the 2-week run-in period, participants will receive a variable duration BCT intervention, and the length of the intervention is determined by utilization of the modified TiTE-CRM design. During the BCT intervention, participants will receive 5 daily BCTs via text message. Content of the text message will be specific for each BCT (e.g. a Goal Setting text message will encourage participants to develop a walking goal for the day). Initially, 3 participants will be treated at a moderate dose level, which is five weeks of the multi-BCT intervention to increase PA. Based on the calculated MED for the first cohort, subsequent cohorts will be administered a longer or shorter dose of the intervention. The BCT dose for each cohort will be determined by the study statistician based on the proportion of individuals in the prior cohort exhibiting the target behavior (in this case, a 2,000 step per day increase between baseline and follow-up periods). As the MED involves comparing PA levels between the run-in and follow-up periods, participants will not be assigned to subsequent cohorts unless all of the participants in the prior cohort have completed some of the intervention period. The treatment response for the prior cohort will be used to guide the dose administered to the subsequent cohort using modified TiTE-CRM methodology.

Following the completion of the intervention, all cohorts will be assessed for a 2 week follow-up period. Follow-up consists of wearing the activity monitor continuously, and use of electronic pill bottle to assess adherence. No interventions will be delivered during this period. At the end of the study, participants will be asked to complete the same questionnaire completed during baseline and the intervention phase as well as a satisfaction survey regarding the BCT intervention. Participants will also be reminded/instructed to return their eCAP smart pill bottle to the study team via addressed packaging included in their study materials.

12. STATISTICAL ANALYSIS

- *Describe how your data will be used to test the hypotheses.*
- *State clearly what variables will be tested and what statistical tests will be used.*
- *Include sample size calculations.*
- *If this is a pilot study, state which variables will be examined for hypothesis generation in later studies.*

Analysis for the Primary Aim: The minimum effective dose (MED) will be defined as the smallest BCT dose duration associated with a successful PA increase (defined as an average increase of 2,000 steps per day) between the 2-week run-in and 2-week follow-up periods in at least 80% of participants. The MED will be estimated based on the modified TiTE-CRM, which is an adaptive model-based, dose-finding design for estimating the maximum tolerated dose in pharmacologic agents. In this study, we will adapt the TiTE-CRM for the purpose of MED estimation. Briefly, the TiTE-CRM operates as follows during a study. Participants will be enrolled in cohorts of 3. The first cohort will be given a BCT intervention with a duration of 5 weeks. Subsequent cohorts will be given a BCT intervention duration (from 1-week to 10-week) based on the updated MED estimate according to the modified TiTE-CRM model and data from the previously enrolled participants. The process will continue until we reach a total of 42 participants (14 cohorts) randomized to the intervention. Once the study has completed enrollment, we will identify which dose of the BCT intervention (in weeks) is associated with ≥80% of participants achieving the goal of an average of 2,000 steps per day increase between the baseline and follow-up periods. Means and standard deviations of step scores for baseline versus behavioral change strategy treatment period will be visualized using a column graph. The statistical significance of differences will be adjusted for time interval. The effects of treatment on number of steps will be assessed using generalized linear mixed models (GLMM). This model will account for possible autocorrelation and linear trends between steps across time.

Analysis for Secondary Aim 1: To identify estimates of the indirect effect of the BCT intervention on PA via potential mediator MoAs, we will conduct the analysis in 3 steps using mixed effects regression models. First, we will estimate the direct effect of the BCT intervention on PA. Second, we will estimate the effect of the BCT intervention on each potential MoA. Third, we will estimate the indirect effect of the BCT intervention on PA.

Analysis for Secondary Aim 2: The effect of the multi-BCT intervention on adherence to statins will be examined across the study duration. Participant steps will be assessed continuously using a Fitbit mobile device. Daily steps for participants will be aggregated by run-in and follow-up periods to generate average daily steps in each period. Changes in daily steps between run-un and intervention periods will be compared using Generalized Linear Mixed Model Analyses.

Analysis for Exploratory Aim: Participant heterogeneity in amount of time required to reach a successful increase in daily steps (defined as an increase of 2,000 or more steps per day over a 2-week period compared to run-in) will be examined. Average step counts will be calculated for each 2-week block during the intervention and follow-up periods. Average steps per day in these blocks will be compared with the average daily steps in the run-in period. Once a successful increase has been detected, the time to achieve this treatment response will be recorded. Differences in duration

to successful increases in physical activity will be examined between participants using mixed effects regression models.

The sample size of 42 participants randomized was chosen to have a sufficient number of participants to obtain a preliminary assessment of the MED for the five-component behavioral change intervention to increase walking between baseline and follow-up periods. The duration of dose and number of measurements/reports were based on expert recommendations and estimations about maximal duration of the trial to maintain patient engagement. Data will be reported transparently so that individual level heterogeneity can be assessed.

The dose-efficacy model is calibrated such as that the modified TiTE-CRM will eventually select a BCT duration associated with 75%-85% successful PA success, i.e., within 5 percentage points of our target [30]. The sample size (n=42) is determined to achieve 60% probability of correct selection (PCS) under logistic dose-efficacy curves with slope = 0.69 (i.e., an OR = 2) [31]. As this is small-scale pilot study, power and sample size will be calculated solely for the primary aim.

13. SPECIMEN BANKING

- *If specimens will be banked for future research, describe where the specimens will be stored, how long they will be stored, how they will be accessed and who will have access to the specimens*
- *List the information that will be stored with each specimen, including how specimens are labeled/coded*
- *Describe the procedures to release the specimens, including: the process to request release, approvals required for release, who can obtain the specimens, and the information to be provided with the specimens.*

N/A

14. DATA MANAGEMENT AND CONFIDENTIALITY

- *Describe the data and specimens to be sent out or received. As applicable, describe:*
  - *What information will be included in that data or associated with the specimens?*
  - *Where and how data and specimens will be stored?*
  - *How long the data will be stored?*
  - *Who will have access to the data?*
  - *Who is responsible for receipt or transmission of data and specimens?*
- *Describe the steps that will be taken to secure the data during storage, use and transmission.*

Fitbit

This pilot study uses commercially available, non-NFC, Fitbit devices to remotely monitor participant activity. All enrolled participants will be provided with a study account that has been created by the research team with no identifying information to the participant. The email address of the study account contains a unique identifier

(e.g. northwellf25). Data collected will include daily steps, floors climbed, activity intensity, sleep duration, battery life, last sync, and estimated minutes in sleep stages. A file linking the Fitbit identifier to the study participant will be housed in a Northwell-approved drive to store PHI, and be accessible only by members of the study team listed in the IRB application. Coded data from Fitbit will remain stored in a Northwell-approved drive indefinitely.

Fitabase

This pilot study will use Fitabase to retrieve Fitbit data from participants. Fitabase is a secure, online portal. The Fitbit study account provided to the participants will be linked to an identification number in the Fitabase system (e.g. FLT01). No information that could be used to identify a participant will be stored on Fitabase. Only the research team will have access to data that will be able to connect a research participant to their Fitabase ID. Data collected will include last sync date, battery charge status, daily steps, floors climbed, activity intensity, sleep duration, and estimated minutes in sleep stages. Fitabase will stop tracking participant data at the trial end date selected by the research coordinator. As an added measure, participants will be instructed to remove the Fitbit study account from their device if they plan on keeping the Fitbit.

Medication Adherence

We will monitor daily adherence to clinically prescribed statins using the eCAP smart pill bottle by Information Mediation Corporation. eCAP smart pill bottles are a type of medication adherence tracking device. The eCAP is an electronic content monitor (ECM) that tracks medication usage without active participant input and without the use of any downloadable app. While the eCAP ECM system does have the capability to integrate with android or iOs phones, the study team will not utilize this feature. eCAP stores information about the opening of the pill bottle but no patient information or identifying data is stored on the device. Compliance data will be available for download by the study team upon receipt of the eCAP smart pill bottle at the end of the research.

Eligibility, Consent, and Survey and Fitbit Data

Survey and Fitbit data will be collected and stored using RedCap, which is a Northwell security-review approved system for collecting and storing research data, including PHI. The study team will have access to all data, including PHI, throughout the study. Pooled results will be used to assess gaps in phenotypic understanding to empirically determine if modeling precise therapy is feasible.

The study team takes data confidentiality very seriously. Data collected for this research will be maintained on a HIPAA-compliant Northwell-approved SQL database. All members of the research team with access to identifiable and coded data will be trained and included on the IRB submission for approval. Regular meetings will take place with the PI and other members of the study team to ensure protocol adherence and data accuracy. Data collected for this study will be maintained in its original and unaltered source data state in a Northwell-approved SQL database on a Northwell-approved drive to store PHI indefinitely. Data collected under this research may be used for future research in coded format without additional consent as per the consent form participants sign and with appropriate IRB approval as required. Any additional data that must be shared will be done so

according to the consent form participants signed. Only research staff listed within this IRB submission will have access to identifiable information. Anonymized data may be stored indefinitely for reference following the conclusion of the study. The participant will be made aware of all data collected in the consenting process.

This research is funded by the NIH, thus a Certificate of Confidentiality has been issued for this research. Certificates of Confidentiality (CoCs) protect the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations.

15. DATA AND SAFETY MONITORING PLAN

A specific data and safety monitoring plan is only required for greater than minimal risk research. For guidance on creating this plan, please see the Guidance Document *on the HRPP website.*

Part I – this part should be completed for all studies that require a DSMP.
Part II – This part should be completed when your study needs a Data and Safety Monitoring Board or Committee (DSMB/C) as part of your Data and Safety Monitoring Plan.

Part I: Elements of the Data and Safety Monitoring Plan

- *Indicate who will perform the data and safety monitoring for this study.*
- *Justify your choice of monitor, in terms of assessed risk to the research subject's health and well being. In studies where the monitor is independent of the study staff, indicate the individual's credentials, relationship to the PI, and rationale for selection*
- *List the specific items that will be monitored for safety (e.g. adverse events, protocol compliance, etc)*
- *Indicate the frequency at which accumulated safety and data information (items listed in # above) will be reviewed by the monitor (s) or the DSMB/C.*
- *Where applicable, describe rules which will guide interruption or alteration of the study design.*
- *Where applicable, indicate dose selection procedures that will be used to minimize toxicity.*
- *Should a temporary or permanent suspension of your study occur, in addition to the IRB, indicate to whom will you report the occurrence.*

Given that study activities involve no more than risks encountered in daily life (increased time spent walking by healthy, working individuals), the study has received approval from the NIA for a safety monitor. Dr. Zenobia Brown has been approved to provide safety monitoring for this pilot. Dr. Brown is a family medicine clinician and oversees Northwell's Health Solutions programs.

Part II: Data and Safety Monitoring Board or Committee

- *When appropriate, attach a description of the DSMB.*

- *Provide the number of members and area of professional expertise.*
- *Provide confirmation that the members of the board are all independent of the study.*

Given that study activities involve no more than risks encountered in daily life (increased time spent walking by healthy, working individuals), the study has not convened a DSMB.

16. WITHDRAWAL OF SUBJECTS

- *Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent*
- *Describe procedures for orderly termination*
- *Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.*

Circumstances under which participants will be withdrawn from the research without their consent include failure to maintain protocol adherence and repeated failure to complete the assigned BCT intervention.

Potential participants will be notified of the possibility of being removed from the study before or during the BCT intervention phase due to adherence issues in the informed consent. Participants who fail to maintain minimum adherence during baseline will be notified by the research team after 10 days of baseline participation.

Participants who fail to maintain protocol adherence or who deviate from the protocol will be contacted by a member of the study team with a reminder of the study protocol, and warning that this may impact their continued study eligibility. Once a protocol deviation has been repeatedly recorded, the Principal Investigator will determine the participant's continued eligibility in the study, with consultation of the Safety Officer if needed. If it is determined that the participant will be withdrawn from the study, the participant will be notified by the research team via email and phone call. The participant will stop receiving notifications and survey prompts, and will be sent instructions to un-link their Fitbit device. The participant will be able to keep their Fitbit device but will be required to return their eCAP smart pill bottle.

Participants may withdraw from participation in the research at any time. Given the non-invasive nature of study-specific monitoring, there are no significant anticipated direct adverse effects related to withdrawal. Participants may easily elect to withdraw by emailing Research personnel directly at:

Dr. Catherine Alfano
130 East 59th Street, Suite 14C
New York, NY 10022
stepcohort@northwell.edu

If a participant withdraws from the study, previously collected data will not be deleted. However, no new information will be collected from a participant after he/she has withdrawn from the study. We will clarify how to transfer the Fitbit

to a personal account and will ask participants to complete a satisfaction survey at the time of their withdrawal (as proposed for all participants who complete the research) to tell us about their experience in the study. The participant will be sent an electronic survey including questions regarding their experience during the study, or will be contacted by phone or teleconference if they do not complete the electronic survey. Completion of this survey is voluntary and will help us design better research in the future.

Participants will be considered to be "active" until we are notified of their request to terminate participation.

17. RISKS TO SUBJECTS

- *Describe any potential risks and discomforts to the subject (physical, psychological, social, legal, or other) and assess their likelihood and seriousness and whether side effects are reversible. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.*
- *Include risks to others , like sexual partners (if appropriate)*
- *Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to results*
- *Describe the procedures for protecting against or minimizing any potential risks, including risks to confidentiality, and assess their likely effectiveness.*

This study poses low risk of physical harm to subjects.

One risk of taking part in this study is the possibility of a loss of confidentiality or privacy. The study team plans to protect privacy by only sharing necessary information about participants to those outlined in the consent form. All subjects will be informed that their responses are confidential and that they may refuse to participate in the project or withdraw at any time without explanation, and that such action will not affect their future interactions with their health care providers, employment, educational studies, or the research study. The risk of loss of confidentiality will be minimized by securely storing data including PHI in a Northwell-approved database and minimizing the use of PHI.

There is no additional risk with using a Fitbit activity monitor for research as compared to using the device as a consumer, including mild skin irritation (i.e. contact dermatitis) which occurs among a small proportion of users. Participants will be instructed via the consent form on methods to reduce irritation (i.e. keep the band clean and dry) and that they can remove the band for a short period of time.

There are no known risks associated with utilization of the BCTs employed in this intervention. It is possible that messages prompting physical activity may cause mild stress in participants who are ambivalent about increasing their step count. Increasing step count by 2,000 steps per day in ambulatory persons without mobility impairments or safety limitations represents no more than minimal risk. Mild symptoms of increased activity such as fatigue or muscle soreness may be experienced.

There are no known risks to utilizing eCAP smart pill bottle. The vial smart cap meets all federal stands for safety (childproof). No patient information or identifying data is stored on the device. There is no GPS tracking from the eCAP device.

The proposed questionnaires are not anticipated to pose risk to the participants. Participants will receive text message notifications with a secure link to a survey that can be can be accessed via a smartphone. All survey responses will be directly entered by participants in an electronic format (secure, HIPAA compliant RedCap database).

18. RESEARCH RELATED HARM/INJURY

- *Describe the availability of medical or psychological resources that subjects might need as a result of anticipated problems that may be known to be associated with the research.*
- *If the research is greater than minimal risk, explain any medical treatments that are available if research-related injury occurs, who will provide it, what will be provided, and who will pay for it.*

Research-related injuries are not expected for this no greater than minimal risk project.

19. POTENTIAL BENEFIT TO SUBJECTS

- *Explain what benefits might be derived from participation in the study, noting in particular the benefit over standard treatment (e.g. a once-a-day administration instead of four times a day, an oral formulation over an IV administration).*
- *Also state if there are no known benefits to subjects, but detail the value of knowledge to be gained*

Participating could improve physical activity and subsequently reduce cardiovascular risk. In addition, the information collected from participant involvement will inform the development of future BCTs to help other research participants, and eventually patients, discover which behavioral treatment options are best for them as an individual.

20. PROVISIONS TO PROTECT PRIVACY INTERESTS OF SUBJECTS

- *Describe the methods used to identify potential research subjects, obtain consent and gather information about subjects to ensure that their privacy is not invaded.*
- *In addition consider privacy protections that may be needed due to communications with subjects (such as phone messages or mail).*

The study will be advertised to potential participants via established Northwell communication channels, including via NWH secure email and secure communication with Quantitative Intelligence (QI). Inter-departmental support has been shown across Northwell to assist the researchers in meeting recruitment goals. Their extensive electronic communication system will allow for the rapid delivery of recruitment materials directly to potentially-eligible participants.

Recruitment links will lead to a study web page asking potential participants to sign authorization to undergo brief screening to assess if they are eligible for participation and to provide demographic information needed to comply with NIA regulations. Participants who authorize the study team will be provided with more information about study requirements, eligibility, and who to contact for more information. Interested individuals will be asked to sign consent via a 21 CFR Part 11 and HIPAA compliant Northwell Health approved electronic platform. Individuals may call the research team at any time to ask questions prior to signing consent. Should this occur, research personnel will ensure that the individual is in a private location for open conversation to protect the privacy interests of the individual. All study-related communications will be delivered via a secure, NWH email or via the NWH approved e-platform.

21. COSTS TO SUBJECTS

- *Describe any foreseeable costs that subjects may incur through participation in the research*
- *Indicate whether research procedures will be billed to insurance or paid for by the research study.*

This research study is funded by the National Institutes for Health (NIH). All study related devices will be provided to participants at no cost. Participant insurance will not be billed.

This study uses text messaging to deliver notifications, reminders, and study questionnaires. Standard message and data rates from the participant's wireless carrier may apply to the study participant. Study participants will not be compensated for any costs related to data usage or sending or receiving text messages by the study or by members of the study team.

22. PAYMENT TO SUBJECTS

- *Describe the amount of payment to subjects, in what form payment will be received and the timing of the payments.*

There is no payment to subjects for participation in this research, however participants will be allowed to keep their Fitbit device if they –are randomized to the intervention phase.

23. CONSENT PROCESS

If obtaining consent for this study, describe:

- *Who will be obtaining consent*
- *Where consent will be obtained*
- *Any waiting period available between informing the prospective participant and obtaining consent*
- *Steps that will be taken to assure the participants' understanding*
- *Any tools that will be utilized during the consent process*
- *Information about how the consent will be documented in writing. If using a standard consent form, indicate such.*
- *Procedures for maintaining informed consent.*

Each subject will receive written explanations of the purposes, procedures, and risks of this study in language appropriate for the individual's level of understanding. All questions will be answered via email or phone, and if all inclusion criteria are met, and the subject volunteers to participate, digital written informed consent will be obtained.

Written, electronic consent (e-consent) will be obtained via REDCap, a web-based platform capable of recording electronic signature. The e-consent document will contain all of the elements of informed consent required by applicable federal regulation for the protection of human subjects and elements of authorization required by the HIPAA Privacy Rule, and will begin with a concise and focused presentation of the key information that is most likely to assist participants in understanding the reasons why he/she might or might not want to participate in the research.

Because consent will be obtained remotely, the electronic platform will be designed such that the consent form is easy to navigate. The system will also incorporate electronic strategies to encourage participants to access all of the consent material before documenting his/her consent.

We will also employ interactive electronic-based technology such as a comprehensive knowledge check at the end of the consent process. Participants may contact a member of the research team with questions about the research. Both the research phone and email inbox will be monitored daily by consenting coordinators.

PDF copies of signed consent forms will be electronically stored in a HIPAA-secured, Northwell approved storage drive with protected access to only the PI and research personnel listed on the study protocol.

In the state of NY, any participants under the age of 18 are considered children. If your study involves children, additional information should be provided to describe:

- *How parental permission will be obtained*
- *From how many parents will parental permission be obtained*
- *Whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. The process used to determine these individual's authority to consent for the child should be provided*
- *Whether or not assent will be obtained from the child*
- *How will assent be documented*
- *Whether child subjects may be expected to attain legal age to consent to the procedures for research prior to the completion of their participation in the research. If so, describe the process that will be used to obtain their legal consent to continue participation in the study. Indicate what will occur if consent is not obtained from the now-adult subjects.*

If the study involves cognitively impaired adults, additional information should be provided to describe:

- *The process to determine whether an individual is capable of consent*
- *Indicate who will make this assessment*
- *The plan should indicate that documentation of the determination and assessment will be placed in the medical record, when applicable, in addition to the research record.*
- *If permission of a legally authorized representative will be obtained,*
  - *list the individuals from who permission will be obtained in order of priority*
  - *Describe the process for assent of subjects; indicate whether assent will be required of all, some or none of the subjects. If some, which subjects will be required to assent and which will not.*
  - *If assent will not be obtained from some or all subjects, provide an explanation as to why not*
  - *Describe whether assent will be documented and the process to document assent*
  - *Indicate if the subject could regain capacity and at what point you would obtain their consent for continued participation in the study*

If the study will enroll non-English speaking subjects:

- *Indicate what language(s) other than English are understood by prospective subjects or representatives*

- *Indicate whether or not consent forms will be translated into a language other than English*
- *Describe the process to ensure that the oral and written information provided to those subjects will be in that language*
- *If non-English speaking subjects will be excluded, provide a justification for doing so*

The study is committed to enrolling a racially and ethnically diverse population. We anticipate that most participants will have the competency to comprehend study materials produced in the English language at a 6th grade level, particularly when explained by trained clinical research coordinators. Exclusion of non-English speaking participants in this pilot study will not later negatively impact equitable access, participant comprehensibility or research design applicability to the diverse populations that may be solicited for participation in future clinical trials.

24. WAIVER OR ALTERATION OF THE CONSENT PROCESS ☐ N/A

Complete this section if you are seeking an alteration or complete waiver of the consent process.

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk to the subject:*
- *Explain why the waiver/ alteration will not adversely affect the rights and welfare of subjects*
- *Explain why it is impracticable to conduct this research if informed consent is required*
- *Explain why it is not possible to conduct this research without using the information or biospecimens in an identifiable form*
- *If appropriate, explain how the subjects will be provided with additional pertinent information after participation. If not appropriate to do so, explain why.*

Since the consent process will be remote and self-directed, it is not practicable or feasible for the investigator to sign the consent form in REDCap. As such, we request a waiver of the investigator's signature for this research which is no greater than minimal risk. Individuals are encouraged to reach out to the study team via email and/or a direct phone line if they have any questions and prior to signing the consent form.

Complete this section if you are obtaining informed consent but you are requesting a waiver of the documentation of consent (i.e., verbal consent will be obtained). *To proceed with a waiver based on these criteria, each subject must be asked whether they wish to have documentation linking them to this study.* ***Only complete subsection 1 OR subsection 2.***

SUBSECTION 1

- *Explain how the only record linking the subject to the research would be the consent document.*

- *Explain how the principal risk of this study would be the potential harm resulting from a breach in the confidentiality*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

SUBSECTION 2

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk.*
- *Confirm that the research only involves procedure for which consent is not normally required outside the research context.*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

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25. WAIVER OF HIPAA AUTHORIZATION ☒ N/A

Complete this section if you seek to obtain a full waiver of HIPAA authorization to use and/or disclose protected health information.

- *Describe the risks to privacy involved in this study and explain why the study involves no more than minimal risk to privacy:*
- *Describe your plan to protect identifiers from improper use or disclosure and to destroy them at the earliest time.*
- *Indicate why it is not possible to seek subjects' authorization for use or disclosure of PHI.*
- *Indicate why it is not possible to conduct this research without use or disclosure of the PHI.*
- *Indicate if PHI will be disclosed outside NSLIJ Health System, and if so, to whom. Note: PHI disclosed outside NSLIJ Health System, without HIPAA authorization needs to be tracked. Please see guidance at www.nslij.com/irb for information about tracking disclosures.*

Complete this section if you seek to obtain a partial waiver of the patient's authorization for screening/recruitment purposes *(i.e., the researcher does not have access to patient records as s/he is not part of the covered entity)*

Note: Information collected through a partial waiver for recruitment cannot be shared or disclosed to any other person or entity.

- *Describe how data will be collected and used:*
- *Indicate why you need the PHI (e.g.PHI is required to determine eligibility, identifiers are necessary to contact the individual to discuss participation, other)*
- *Indicate why the research cannot practicably be conducted without the partial waiver (e.g. no access to medical records or contact information of the targeted*

population, no treating clinician to assist in recruitment of the study population, other)

26. VULNERABLE POPULATIONS:

Indicate whether you will include any of these vulnerable populations. If indicated, submit the appropriate appendix to the IRB for review:

- ☐ *Children or viable neonate*
- ☐ *Cognitively impaired*
- ☐ *Pregnant Women, Fetuses or neonates of uncertain viability or nonviable*
- ☐ *Prisoners*
- ☒ *NSLIJ Employees, residents, fellows, etc*
- ☐ *poor/uninsured*
- ☐ *Students*
- ☒ *Minorities*
- ☐ *Elderly*
- ☐ *Healthy Controls*

If any of these populations are included in the study, describe additional safeguards that will be used to protect their rights and welfare.

The Institute of Health System Science (IHSS) has established a good working relationship with Northwell Health Employees. From our past enrollment of NWH workforce, multiple individuals have expressed interest in participating in future IHSS trials, including pilots like this one. As such, Northwell Health Employees are ideal study subjects for this research.

All data, including this participant information, will be maintained by the study team on a Northwell-approved drive to store PHI. All members of the research team with access to identifiable and coded data will be trained and included on the IRB submission for approval.

The research will not interfere with NWH employees' job obligations. An employee's decision to participate or not participate will have no bearing on the employee's performance evaluation or employability at NWH. In addition, participants will be able to withdraw from the study at any time, for any reason without influencing their ability to receive health care and/or affect their employment status.

We do not intend to prevent study personnel or other employees of the Institute of Health System Science who express an interest in the research from participating. However, no supervisory personnel will be able to enroll participants who report to them in this research. We are not intentionally targeting minorities, but expect minorities to be part of those eligible for participation.

27. MULTI-SITE HUMAN RESEARCH (COORDINATING CENTER)

If this is a multi-site study where you are the lead investigator, describe the management of information (e.g. results, new information, unanticipated problems involving risks to subjects or others, or protocol modifications) among sites to protect subjects.

N/A

28. REFERENCES/BIBIOGRAPHY

Provide a reasonable list of references directly related to the study. Any diagrams for new medical devices or brief reprints from journals might also prove useful.

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