Northwell Health

RESEARCH PROTOCOL

Protocol Title:	Influencing Basic Behavioral Mechanisms of Action while targeting Daily Walking in Those at Risk for Cardiovascular Disease: Science of Behavior Change Factorial Experiment of Behavioral Change (MOST 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:
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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*

Increasing physical activity (PA) in sedentary people at risk for cardiovascular disease related to elevated blood pressure, elevated body mass index (BMI) high cholesterol levels or other CVD risk factors such as diabetes and smoking is of high public health significance. This study will advance knowledge about which behavior change techniques (BCTs) are most important for behavior change to reduce sedentary behavior. The study applies an experimental medicine approach to identify and assess the mechanism of action (MoA) potentially underlying a physical activity behavior change. The study hypothesizes that self-efficacy for physical activity will significantly impact the relationship between each one of 4 BCTs (randomly introduced) used in the study and increased walking behavior at 6 months

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*

The U.S. population has experienced a shift in the causes and types of diseases that compromise quality and quantity of life.(1) The prevalence of "degenerative and man-made diseases" has increased.(2) And, recent estimates reveal a slowdown in the decline of these chronic diseases' occurrence and impact; we are experiencing worse health, and for some, shorter lives.(3) Rates of myocardial infarction, stroke, and other cardiovascular disease (CVD) events have plateaued,(4) but are common, costly, and preventable events. From 2016 to 2021, 3.3 million per year of these preventable events are projected to occur, including 2.2 million emergency visits, 2.1 million deaths, and 11.8 million hospitalizations. These preventable events would result in estimated care costs of $170 billion, with about half of these events projected to occur among 18- to 64-year-old adults.(5) Although the reasons are complex for the plateau in CVD incidence, Mokdad and others provocatively suggest that the main causes of death in the U.S. are now behavioral.(6-7) Although tobacco use is the biggest cause, physical (in)activity and poor diet combined are the second most common causes. Physical inactivity and poor diet are projected to soon overtake tobacco as the leading cause of death for Americans.(1-2) Consistent with these projections, improvements in several protective factors, such as engaging in regular physical activity (PA), have stalled in recent years for most American adults,(8-9) although any increase in activity is preventive of future disease.(10-11) For those at risk for CVD, all major guidelines and recommendations include the importance of adults engaging in regular PA.(12-15) And, engaging in even low-intensity PA improves intermediate outcomes 8,6 that, in turn, prevents CVD in those at risk for developing CVD.(13) In the National Health Interview Study (2016), physical inactivity was defined as not even engaging in light leisure-time PA for at least 10 minutes, 29% of all adults reported that they were inactive (16) Hence, an estimated 71 million adults do not engage in even 10 minutes of leisure-time or very low-intensity PA.(16) This extreme level of physical inactivity is higher among women (31%) than among men (27%), and is higher among blacks (37%) and Hispanics (36%) than among whites (26%).(17) For those 18-64 years of age, many of whom are starting to be at elevated risk for CVD,(16) physical inactivity prevalence is estimated to be 28%.18 Thus, millions of Americans will likely develop a preventable disease—CVD. Evidence indicates that those who engage in even low-intensity PA are at less risk for developing CVD, and that PA is already recommended to the millions who are inactive. But few in the U.S. regularly engage in any level of intensity of PA.(16) . Observational evidence has accumulated that low-intensity PA can confer health benefits(19) Currently inactive persons, who increase even their low intensity activity, will benefit.(19)Those who walk 1000-1900 steps per day, versus 0-1000 steps per day have a lower mortality rate.(20) As a result, interest has grown for increasing even low-intensity activity. Fewer behavior change PA interventions, but still many, have focused on low-intensity activity, or walking,(21-23) with some reporting that even an increase of 1000 steps per day at low-intensity is associated with a 7% reduction in death and a 3% reduction in hospitalization in patient populations (e.g., heart failure patients), after controlling for traditional predictors of these endpoints.24 The addition of some efficacious, low-intensity PA interventions, at least for currently sedentary populations is warranted(19) Guidelines both to

promote physical activity (PA)(12) and prevent CVD recommend behavioral counselling to increase moderate-to-vigorous PA.(15-17) And, although engaging in moderate-to-high intensity PA improves intermediate outcomes (19,10) that, in turn, prevent CVD,(13) adherence to these recommended levels of moderate intensity PA is poor,(21,25) and has plateaued.(26) As a result, persons at risk for CVD, who receive full guideline-based physical activity counselling, remain predominately sedentary, and continue at increased risk for morbidity and mortality, compared to their more active counterparts.(26) Hundreds of BCT interventions support the efficacy of walking and other low-intensity PA interventions.(27-29) But these interventions have predominantly included a combination of many BCTs, and so cannot identify the individual effect for each BCT on the resulting behavior change.(29) Further, these multi-BCT randomized interventions, although usually stating the mechanism of action (MoA) hypothesized to play a causal role in producing behavior change, did not actually test whether the MoA was engaged, and whether it, in turn, influenced the behavior.(30 -32) The benefits of even low-intensity PA,(18) the poor adherence to higher intensity PA interventions, and the inefficiency of using multi-BCT RCTs to elucidate the efficacy of individual intervention components, all argue for using an experimental medicine approach to determine which BCTs influence self-efficacy, and in turn, improve walking. This is the gap in basic behavioral mechanism research that we will address.

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.*

We will use a randomized, factorial experiment utilizing the Science of Behavior Change (SOBC) approach to efficiently test the effects of four distinct behavior change techniques (BCTs) thought to engage one key behavioral mechanism of action (MoA) for improving daily walking by at least 1000 steps per day. **Overarching Aim:** Conduct a randomized factorial experiment to test a mediational model of four BCTs targeting changes in self-efficacy for PA, which are, in turn, hypothesized to cause increased walking in sedentary adults, 18 to 74 years of age who are at risk for CVD. **Hypothesis:** Self-efficacy for physical activity (mediator) will significantly mediate the relationship between randomization to each BCT (independent variable) and increased walking (dependent variable) at 6 months. **Exploratory Aim:** Explore effect moderation in the mediational model of the BCTs by actual use or enactment of a BCT and for whom and under what conditions mediation occurred.

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*

Given that this study is conducted virtually, the opportunity for enrollment is widely available.. National statistics support both the prevalence of sedentary behavior (enhanced by the pandemic) and elevated risk for cardiovascular disease in the adult population, allowing for achievement of recruitment milestones over the course of the project. The Institute of Health System Science personnel are experts in the conduct of virtual research using monitoring technology. Staff must meet certain eligibility criteria before implementing 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, Co-I and an additional weekly meeting with the Project Coordinator, 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 Coordinator, Director of Clinical Research, and Principal Investigator to answer any protocol questions they may have outside these established weekly meetings. Weekly meetings with project personnel, under the direction of the PI and including representatives from the Institute's data team will ensure that all implementation, safety and data tasks are performed according to established timelines.

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*

Initial study participants will be recruited electronically through online networks, through dissemination of fliers, and electronic communication updates from Northwell Health Wellness programs. Participants will also be recruited from social media sites and other sources to ensure the widest and most diverse potential participant pool possible. This will include electronic communications throughout the Northwell employee network, which offers research volunteer opportunities to over 74,000 employees. We will use other strategies as needed to ensure that our participant pool is diverse on many dimensions including potentially translating materials into Spanish. The study will also accept referrals from the clincialtrials.gov posting. The study web pages will contain detailed descriptions of

the study, including study objectives, procedures, risks, benefits, voluntary status, privacy and data security assurances. Our group has successfully piloted the creation of in-house videos of skilled clinical research coordinators' discussing all the above, demonstrating study devices and procedures, and facilitating remote study enrollment, with high levels of participant satisfaction.

Participants will have the opportunity to have questions answered by clinical research coordinators via email or text message, or have a video/phone conversation, according to participant preference and comfort level. Once it is confirmed that the participant has no further questions, they will be required to respond to three questions about the study designed to ascertain comprehension of their rights and responsibilities as research participants. Those found eligible and consented will be mailed a FitBit activity monitor, and access to onboarding study instructions.

Participants will receive $100 at the completion of the intervention (Month 3) and $150 for successful study completion. Additionally, they will be able to keep their FitBit, valued at approximately $150. Participants in the study follow-up period (Months 4-6) may be eligible for a random, weekly lottery of $100 should they maintain adherence to Fitbit activity watch wear and responses to texts messages and surveys.

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.*

Participants must be able to read/comprehend English and own a smart phone capable of receiving text messages. Participants must be fully ambulatory and have never been advised that it would be unsafe to participate in a walking program. Individuals with a diagnosis of a serious mental health condition or psychiatric disorder will be excluded. Additionally, individuals who are pregnant or who plan to become pregnant in the 5 months following enrollment will be excluded. Participants must be 18 to 74 years of age, sedentary, and have a risk factor for CVD. Sedentary behavior will be assessed via potential participants' self-reports during screening and confirmed by the FitBit Fitness Tracker, during the four week baseline run-in period. To define 'at risk for CVD' we will follow the criteria of the

United States Preventive Services Task Force: www.uspreventiveservicestaskforce.org. These are: diagnosed hypertension, dyslipidemia, body mass index ≥ 30, diabetes or pre-diabetes, or 10-year CVD risk > 7.5 (using the Pooled Cohort Equations or Framingham Risk Score). Potential participants will be considered sedentary, if, in the baseline period, they are considered objectively sedentary, and they will be considered adherent if they have ≥ 10 hours of device wear time and answer daily texts on at least 21 of the 28 days of the baseline period, submit 3 onboarding surveys, and submit at least 1 of the 3 self-efficacy surveys sent via text message during the baseline period.

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.*

The study plans to enroll 820 participants. It is anticipated 624 will successfully complete baseline and be randomized, and that 480 participants will complete the trial

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*

Individuals will participate in the study for a total of 24 weeks. Four weeks of baseline monitoring of physical activity level and 2 months of study intervention (randomization to one of 15 possible combinations of behavior change techniques or the control group receiving no BCTs, delivered via daily text message with a link to a secure survey) and 3 months of follow-up monitoring. It is estimated that the last participants will be enrolled in September, 2025 to ensure study completion by March 31, 2026

10. ENDPOINTS

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

Self-efficacy for physical activity (mediator) will significantly mediate the relationship between randomization to each BCT (independent variable) and increased walking (dependent variable) at 6 months

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 who self-identify as sedentary will be directed to an information screen with details about the study. Those who are interested in participating in this study will provide basic contact information and demographics and complete general inclusion/exclusion screening criteria. They will then be directed to sign a HIPAA Authorization form before completing the screening survey process that includes additional validated questions pertaining to inclusion and exclusion criteria. Participants with answers that make them ineligible will be directed to a page thanking them for their interest but informing them that they do not qualify for participation in this study. Those who are eligible will receive an electronic copy of the consent form. After reviewing the study overview, potential participants may speak or email study personnel to ensure all their questions are answered. Before being able to sign and submit the consent form, potential participants must demonstrate understanding of the protocol by correctly answering 3 questions pertaining to the information presented in the consent form. The participant will electronically sign the consent form via RedCap which meets 21 CFR 11 standards for collecting electronic signature. A consenting coordinator will review this information and send the potential participant an email which will include a copy of their signed consent form and HIPAA Authorization, as well as information explaining what to expect during onboarding to the study if eligible. They will be mailed an initial study kit with a Fitbit Activity Tracker device. Potential participants will be asked to download the Fitbit app to their smart phone. All baseline periods will begin on a Monday.

The baseline period will take place over the course of 4 weeks. Potential participants will not receive any interventions during this period, but they will be sent a daily text asking them to acknowledge that they have received the message. During the baseline period, potential participants will be asked to wear their Fitbit for at least 10 hours or more per day. Baseline participants will be instructed to sync their Fitbit device by opening the Fitbit app on their phone at least every 24 hours. Participants will receive a bi-weekly self-efficacy survey and three

onboarding surveys assessing neighborhood walkability, social support, and comorbidities.

After completing 28 days in the baseline period, a consenting coordinator will review individual adherence to Fitbit wear. Adherence to Fitbit wear will be defined as recorded heart rate data for at least 10 hours a day. Survey adherence will be defined as submission of a given survey. Baseline participants that do not achieve at least 75% adherence of Fitbit wear, daily survey submission for 21 out of 28 days of the baseline period, and submission of 3 onboarding surveys and at least 1 self-efficacy survey will be withdrawn from the study. Those that maintain adherence and are objectively confirmed as sedentary will be randomized to one of sixteen treatment sequences in the study. Participants who are randomized to receive treatment sequences will receive a text message notifying them of their protocol timeline. Enrollment will continue until up to 624 participants have been randomized into one of 16 possible intervention sequences.

Each intervention sequence contains zero to four of the following Behavior Change Techniques: Goal setting, Action Planning, Self-Monitoring of Behavior and Feedback. One group (control) receives no BCT messages. The intervention phase is 8 weeks in duration.

Daily, all randomized participants will receive one text message from N-1-Thrive. It will provide a link to a secure survey. The survey will contain 0-4 BCT interventions. Responses will be coded as BCT enactment.

The *Goal Setting* survey item is: “Is your goal today to walk an extra 1,000 steps more than your baseline average? Responding with a yes or no is BCT enactment. The *Action Planning* survey item is: “Take one minute and plan for today how, where and when you can walk an extra 1,000 steps more than your baseline average. Have you planned for today?” Responding yes/no is BCT enactment.

The *Self-Monitoring of Behavior* survey item is: “Check your fitbit for yesterday. Type in the number of steps you did yesterday.” Entering a number is BCT enactment.

The *Feedback on Behavior* survey item is dependent on whether or not the participant met their walking goal the day prior.
If their goal was not met the survey item is: “Your goal is to walk 1,000 steps more than your baseline average. Yesterday you did not meet your goal. If you think this is incorrect, you can check your step count from yesterday on your fitbit app to confirm.”

If their goal was met the survey item is: “Your goal is to walk 1,000 steps more than your baseline average. Yesterday you met your goal. If you think this is incorrect, you can check your step count from yesterday on your fitbit app to confirm.” Opening the message is BCT enactment.

A study phone number and email address will be available if a participant is concerned about any side effects they are experiencing and wishes to contact the clinical research coordinator.

Participants will be asked to wear their FitBit tracker for a minimum of 10 hours per day. They will also be asked to complete a validated bi-weekly Self-Efficacy questionnaire. Participants that are not in the control arm will be asked to complete a satisfaction with the BCT survey each month.

Participants may receive additional text messages to those outlined above to remind participants to sync their data, charge their Fitbit or answer surveys. We will send study onboarding instructions in multiple text messages, but during the course of the study we will send a maximum of 5 text messages per day including these reminders and the survey questions outlined above.

In the event of an unanticipated circumstance that temporarily prevents a participant from completing study activities (illness, injury, death in the family, etc.), the participant will have the option of pausing their study to resume once their circumstance has been positively resolved.

Participants will complete remote data monitoring after they have gone through one baseline period (four weeks), 8 weeks of randomized exposure to BCTs or control arm messaging, and 12 weeks of follow-up monitoring. Alternatively, a participant may choose to completely withdraw from the study, or be withdrawn from the study by the research team. Participants who seek to withdraw may decide to only partially withdraw from the study: they will continue to wear the Fitbit tracker and allow the study to record and use their step data, but they will receive no text messages or reminders. If participants decide to partially withdraw, they will not be eligible for compensation. Upon completion of data monitoring, participant Fitbit data will no longer be collected by the study team. Daily text messages and survey prompts will be cancelled for participants who are withdrawn from the study.

We will compile the self-reported data from questionnaires, treatment adherence, side effects, and self-efficacy assessments, as well as information from the Fitbit regarding activity (steps, flights climbed and intensity), sleep (duration, estimated sleep stages) for each individual participant.

As per the consent form, de-identified data will be posted on the following data sharing website: https://cos.io/. The Open Science Framework is a free, open-source web application built to provide researchers with a free platform for data and materials sharing. There will be no identifiable data posted to this website or used in future studies.

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.*

Overall Aim: To conduct a randomized factorial experiment to test a mediational model of four BCTs targeting changes in self-efficacy for PA, which are, in turn, hypothesized to cause increased walking in sedentary adults, 18 to 74 years of age at risk for CVD. To achieve this aim, specifically, we will determine, in three steps: (a). Whether randomization to a BCT will result in increased longitudinal self-efficacy for PA; (b).Whether randomization to a BCT will result in increased Fitbit-assessed average daily step counts in the 6th month, compared to the baseline period; and (c). Whether longitudinal self-efficacy mediates increase in walking by performing sequential mediation analysis en bloc, using the natural effects modeling approach. Whereas Step b determines the total effect of a BCT on PA, Steps a and c together establish the natural direct effect of a BCT on PA, and the natural indirect effect mediated via self-efficacy for PA. **Exploratory Aim:** Explore effect moderation in the mediational model of the BCTs by actual use or enactment of a BCT and for whom and under what conditions mediation occurred. Specifically, we will: (a)N. Explore possible baseline moderators (age, identified gender, race, ethnicity, baseline PA, ted in model (c-i): Month-6 self-efficacy neighborhood walkability score, personal history of walking) that moderate self-efficacy mediation; b. Assess whether BCT adherence moderates the mediation.

Primary Analysis -Modified Intent-to-Treat (ITT) Population: These data will include all randomized participants, who have at least one self-efficacy measure post randomization. Accounting for ineligibility (about 24%) after one-month baseline screening, we expect about N=624 in this data set, which will be used in the primary analysis for the Overall Aim. Furthermore, in the modified ITT population, we expect about N=480 will have all twelve self-efficacy outcomes in the completer-only subset. In the modified ITT data and its completer-only subset, the BCT will be recorded as randomized. **As-treated population**: This will consist of the participants as in the modified ITT Population. However, the degrees of BCT adherence will be used to determine the BCT exposure; see Exploratory Analysis below.

Primary Outcomes and Primary Analysis Self-efficacy for physical activity: The SEW_DUR Self-Efficacy Scale for Walking will be sent electronically Bi-weekly throughout the study starting the first day of baseline. Physical activity assessed by Fitbit: The PA of each randomized participant will be measured continuously for 6 months using the FitBit Tracker. The average daily step counts of each month will be used as the primary PA endpoint. Specifically, the primary PA endpoint in the mediation analysis for the Overall Aim will be the increase in average daily step counts at month 6 from baseline. To test the mediational model hypothesis for the Overall Aim, we perform the analysis in three steps: Step A: The

effects of each randomized BCT on the longitudinal self-efficacy for PA will be assessed using linear mixed effects models, which include a random participant effect, fixed BCT effects, a fixed time effect, and fixed BCT-time interactions. For the Overall Aim, we consider additive BCT main effects and additive BCT-time interaction. The effects of a BCT on self-efficacy for PA will be estimated by the coefficient of the interaction term. As sensitivity analysis, we will perform generalized estimating equations analysis to obtain the robust "sandwich" variance estimation. Step B: The effects of each randomized BCT on average daily step counts at Month 6 will be assessed using linear regression of the four BCTs. Step C: As Step B yields an estimation of the total effect of a BCT on average daily step counts at Month 6, For Step C, natural effects models will be used for effect decomposition into direct effect and indirect effect mediated by increase in self-efficacy relative to baseline. In addition, in order to assess how the timing of increase in self-efficacy mediates BCT effects, we will perform sequential mediation analysis en bloc under the natural effects modeling framework, as follows: We will include increases in self-efficacy at Months 2, 3, 4, 5,and 6 relatively to Month 1 (baseline) in the model, and use them as mediators en bloc. This will give the total mediation effect estimates via all post-randomization self-efficacy, as well as the direct effect of BCT. We will include increases in self-efficacy at Months 2—5 en bloc in the model. This will estimate the mediation effect due to Month 2 to Month 5 self-efficacy. And, by contrasting the indirect effect in this model with that in (c-i), we can estimate the BCT effect mediated by Month 6 self -efficacy alone; right of Figure 3. Likewise, we will proceed to sequentially fit the natural effects model with subsequently fewer self-efficacy mediators. By contrasting the indirect effects in the appropriate natural effect models, this state-of-the-art sequential mediation analysis approach will allow us to identify the self-efficacy mediation pathway temporally. We note that not all pathways are identifiable (e.g., mediation effect of Month 2 self-efficacy that is not through self-efficacy in the later months cannot be identified). Under the natural effect model framework, we will estimate the proportion of mediated effects relative to the total effects.

Sample size calculation: We determined the sample size of this study to have adequate power in Steps A and B in the primary analysis, so that the mediation pathways identified in the primary analysis will likely yield meaningful results. Specifically, we determined the sample size based on power considerations in Step A: We considered conservatively the power of detecting a main BCT effect in linear regression of increase in self-efficacy at one post-randomization time point. (As this is equivalent to fitting a linear mixed effect model of self-efficacy at baseline and one post-randomization time point, the power of the linear mixed effect model that uses self-efficacy at all time points will have more power.) Assuming an effect size of Cohen's d=0.26, to have 80% power for a main BCT effect at 5% significance using Wald test (two-sided), under balanced randomization, we obtained the required total sample size to be N=480. That is, for a given BCT, 240 participants will be randomized to having it, and 240 to not having it; 30 participants will be in each of the 16 BCT combinations. As noted

above, this sample size estimate is conservative, as we anticipate the mixed effects model that used data at all time points in the entire modified ITT population (with N=624) will have substantially greater power. In addition, various meta-analyses estimate the effect size of BCT on self-efficacy for PA to be in the range of 0.19 to 0.26,61,88,100averaged over a wide range BCTs; we used the most recent estimate 0.26 61(Tang et al. 2019) to anchor our sample size determination. Importantly, in this project, because we select BCTs (e.g., Feedback on Behavior) that have shown large effect sizes, we expect the true effect size to be greater than this average of 0.26, and our sample size will yield greater power than 80% in Step A. In the process of determining sample size, we also considered the power for Step B, based on a recent meta-analysis88 that gives an effect size of Cohen's d=0.5. With an effect size greater than that reported for self-efficacy, powering Step A was the driver of sample size. With N=480, the power in Step B is >99% under d=0.5

Analyses for Exploratory Aims Baseline moderators: To explore the moderation effect of baseline variables, such as demographics, we will include the interaction between these and BCTs in the regression models in the sequential mediation analyses described above. To be parsimonious, we will first add baseline variables one at a time, as main effects in the models; only variables that demonstrate significant main effects will be considered in the moderation analysis Joint BCT effects: Leveraging the full factorial experimental design, we will explore (for hypothesis generation) all six possible two-way interactions and four possible three-way interactions among BCTs in the sequential mediation analyses, recognizing that we have limited power to detect anything but a large effect. Effects of BCT adherence: Whether or not a BCT was used on a given day will be determined based on the response to the daily automated texts. For the period spanning from randomization to the end of a given month (say t for t = 2, 3, 4, 5), we will define non-adherence as response rate below 75% for that period. The moderation of adherence (or the lack thereof) will be examined by including an interaction between BCT and its adherence status in the mediation models; due to temporal causation, we will only consider the mediation of self-efficacy after time t. That is, for a given t, we will look at: a: the effects of interaction between each BCT and its adherence up to time t on the longitudinal self-efficacy after time t using linear mixed effects models; b: the effects of interaction between each BCT and its adherence up to time t on average daily step counts at month 6 using linear regression; c: sequential mediation analysis en bloc of self-efficacy after time t. We note that this analysis is equivalent to conducting a mediation analysis under the as- treated population with a main BCT effect coded as 0 for non-adherence.

General Statistical Analytical Approach, Sensitivity Analyses, and Subgroup Analyses Baseline measurements will be summarized with descriptive statistics, including mean, median, and standard deviation for continuous variables (e.g., age) and proportions for categorical variables (e.g., sex, self-identified gender, race/ethnicity). In regression models, all coefficients will be estimated with 95% confidence intervals, and the point estimates, and will be tested using two-sided p values. The modified ITT population will be used for the primary analysis

specified above. To handle missing self-efficacy and step data in the analysis, our primary approach will use last-observation-carried forward (LOCF) imputations. We will also take various analytical approaches for missing data, so as to evaluate how the main conclusions are sensitive to the underlying missing data mechanism. Specifically, for the longitudinal analyses of self-efficacy and BCT (Step A), we will perform the mixed effects models with: 1) observed data only; 2) worst-score imputations; 3) complete data only; and 4) multiple imputations. Note: observed-only analysis (1) is valid under missingness-at-random, whereas complete-data only analysis (3) corresponds to the modified ITT completer-only subset. These four approaches serve as sensitivity analyses to the LOCF analysis and will provide estimates under different missingness assumptions. In addition, we will explore the missingness patterns of self-efficacy data by BCT groups. Similarly, for the analysis of PA and BCT (Step B), we will use these same four methods analogously, in addition to LOCF. For the sequential mediation analysis (Step C), we will adopt methods 2—4 in the natural effect models. We will also perform subgroup analyses by the baseline demographics. In particular, we will test the mediational model by sex-defined subgroup.

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.*

Not applicable

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 study uses non-NFC, Fitbit devices to remotely monitor participant activity and sleep. All enrolled participants will beprovided with instructions to use or create a Google account to log into the Fitbit app with. Data collected will include activity data (daily steps, floors climbed, activity, intensity, heart rate), sleep data (duration/total sleep minutes, sleep and wake times, estimated minutes in sleep stages), and device data (last sync date and Fitbit battery level).

Data Retrieval

This study will retrieve Fitbit data from participants directly from Fitbit or through use of Fitabase. Fitabase is a secure, online portal. The participant's Google account 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.

The Quantitative Intelligence (QI) team at Northwell Health will retrieve participant data directly from Fitbit through an authentication token passed to the Fitbit API, and data resulting from the API call will be stored in an OCIO-approved HIPAA-compliant environment.

The QI team will be provided with participants' study IDs to associate the data to the correct Fitbit account for distribution to the study team.

Data collected from Fitabase and directly from Fitbit will include device data (last sync date, battery charge status), daily activity (steps, floors climbed, activity, intensity, heart rate), sleep data (duration/total sleep minutes, sleep and wake times, and estimated minutes in sleep stages/sleep stage estimates). Both Fitabase and QI will stop tracking participant data at the trial end date selected by the research coordinator.

Intervention Delivery

The study's statistician will create the randomization schedule at the initiation of the study. Only the research team will have access to data that will be able to connect participant name with intervention assignment. The intervention will be delivered by a text with a link to a secure online browser and will be delivered to the individual's personal cell phone. All protocol messaging and data will be delivered/collected via the secure browser (N1Thrive). Data will be stored on the N1Thrive system and delivered back to Northwell via SFTP.

Eligibility, Consent, and Survey Data

Screening and consenting will be done in RedCap. We are partnering with a company (N1Thrive by 4Peacocks) that was formed specifically for the development of technology to support N-of-1 methodology. Survey data will be collected and stored using N1Thrive by 4Peacocks, 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. Coded data using unique generic participant IDs will be shared with 4Peacocks in order to assist with preparing data for analysis by the study statistician..

The study team takes data confidentiality very seriously. The participant will be made aware of all data collected and the companies/technology employed to collect the data via the consent process. Any identifying information will be destroyed once a participant completes their study involvement in the N1Thrive by 4Peacocks database. All data, including 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. Regular meetings will take place with the PI and other members of the study team to ensure protocol adherence and data accuracy.

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.*

This study has been determined by the Northwell IRB to present no more than minimal risks to participants. As such, utilization of a DSMB is not appropriate.

However, attention to data and safety monitoring is of paramount importance to ensure participant safety and data integrity. Primary responsibility for data and safety monitoring will rest with the study physician, Dr. Sal Crusco. Dr. Crusco will ensure medical eligibility and consult with the study exercise physiologist concerning any reported AEs. Dr. Crusco will receive quarterly reports of enrollment numbers and participant demographics, in addition to monthly reports of AEs. Dr. Crusco will provide final approval for the Manual of Operations and all procedures related to ensuring medical eligibility and safe participation in the trial.

The Data Manager (Mr. Vicari), under the direction of the trial's biostatistician Dr. Cheung (Co- Investigator), will provide investigative team with numbers of participants recruited into the trial, demographic breakdowns and reported serious adverse reactions, and data completeness on a monthly basis during team meetings.

The PI, in consultation with the study exercise physiologist and study physician will determine whether unanticipated events are related to the study, whether the study's informed consent form and process needs to be modified, whether the study's procedures need to be modified, and whether the study should be discontinued due to serious adverse outcomes in either the control group or in the intervention groups. All data provided will be provided in a blinded fashion.

There is no provision for early stopping due to efficacy in the primary outcomes. However, as NHLBI will monitor trial progress, they may choose to stop the trial due to safety concerns, not reaching recruitment milestones, much higher drop-out rates than expected, and/or study adherence issues.

How safety will be assessed. The study population will be drawn from a pool of actively working adults, without mobility impairments. Participants with high-risk features as detailed in the exclusion criteria will be excluded to minimize risk. Side effects related to the intervention will be assessed bi-weekly , tracked and reported to the PI and investigative team, IRB and NHLBI according to pre-established policies. All assessments or consultations if needed will be performed by trained personnel

Plan for reporting adverse events. Any adverse event (AE) or unanticipated problem will be identified, responded to, and recorded by the research coordinator, who will in turn ensure that the information is passed on to the study physician. If the AE or problem is unexpected or serious, is related to study involvement, and puts the participant at increased risk, it will be reported to the Institutional Review Board of Northwell Health immediately, in accordance with local policies.

Responsible individual for safety monitoring. The study physician and exercise physiologist (Co-Is Dr. Cruscoand Dr.Friel, respectively) will be responsible for evaluating each AE/problem and determining whether it affects the risk/benefit ratio of the study, and whether modifications to the protocol and consent form are required. Dr.Crusco (Co-I) will be the physician responsible for overall safety monitoring, and will coordinate the training and communication for this function.

Plans for assuring data accuracy and protocol compliance. Dr. Davidson will supervise this study at all times and will be in close and frequent contact with the other Co-Is. In particular, Dr. Davidson will ensure adherence to established federal and institutional patient safety and protection guidelines. To assure data accuracy, Drs. Davidson and Cheung will review the computer data files on a monthly basis. Mr. Vicari (Data Manager) will process the study database monthly to search for errors and generate basic reports for dissemination at regular meetings. Protocol compliance will be reviewed during both weekly meetings between Dr. Davidson, Ms. Duer-Hefele, RN (Director of Operations) and the research coordinators, and during monthly meetings (more frequent if required) between Dr. Davidson and the other co- Is (Drs. Crusco.Friel, Cheung, Suls and Vrany). Finally, Ms. Duer-Hefele will perform a random audit of 5% of study records and provide continual feedback to improve the quality of informed consent and data collection.

We have a number of strategies to ensure the quality of the data. First, the study electronic data entry system we will use “forces” responses to most questionnaire items before allowing progression through the particular assessment’s template, thereby avoiding problems with missing data. For some items, delayed data entry is possible. Further, each time the research coordinator logs into the secure data entry system, it prompts a popup on the initial screen, showing what data elements remain incomplete, to encourage complete data capture.

Wireless data is regularly downloaded from the Fitbit and auto-generated messages are sent to remind participants to charge their device. Text messages and emails will record time of transmission and verification of receipt, and responses where indicated. Research assistants will be able to observe in real time participant unresponsiveness and will contact participants to ensure that they are not experiencing technical difficulties with data collection.

After enrollment of the first 5 participants, Dr. Cheung will examine the data to ensure adequacy and accuracy of data collection. Then, data accuracy will be audited monthly. Finally, as mentioned above, the investigative team will also review data completeness, accuracy, and timeliness on a monthly basis.

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.*

Not applicable

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 self-reported adverse side effects to walking. A potential participant will not be randomized to receive the treatment protocol until he/she has demonstrated at least 75% adherence to continuous Fitbit monitoring (heart rate recorded ≥ 10 hours/day) and response to survey questionnaires during the baseline period.

Potential participants will be notified of the possibility of being removed from the study before treatment randomization 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 21or more 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. 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 and a pre-paid mailer to return their Fitbit device. Participants who are not eligible after baseline because they did not meet objective sedentary behavior criteria will be able to keep their Fitbit and provided instructions how to un-link their device from the study.

Should a participant choose to withdraw from the research study, they will be instructed to send an e-mail to the attention of the Principal Investigator at kdavidson2@northwell.edu or to email mostwalkingsstudy@northwell.edu an e-mail account monitored by IRB-approved members of the research team. They may also message the research team through Twistle. Participants will be contacted by a member of the research team confirming their study withdrawal, and to answer any questions they may have. The participant will stop receiving notification and survey prompts, and will be sent instructions to un-link their Fitbit device. Data collection will stop the day the email is received. All data up until the receipt date of the letter will be included in the research study.

Participants may also decide to "partially withdraw" from the study. This would allow the study to continue to passively collect their step data, but no text messaging would occur. Participants will be provided the following option in Twistle at time of elective withdrawal

Can we continue to collect your fitbit activity data for the remainder of the study? This means that we will continue to see your fitbit activity data but you will not receive any further text messages until the final day of the study. You will no longer be eligible for study compensation.	Yes, you can continue to collect my fitbit activity for the remainder of the study No, you cannot continue to collect my fitbit activity for the remainder of the study. Please fully withdraw me from the study

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.*

Risks of Low-Intensity Walking

Risks of low intensity walking in ambulatory but sedentary individuals may include muscle fatigue and soreness and are generally treatable with rest. Any adverse event (AE) or unanticipated problem will be identified, responded to, and recorded by the research coordinator, who will in turn ensure that the information is passed on to a study investigator. If the AE or problem is unexpected or serious, is related to study involvement, and puts the participant at increased risk, it will be reported to the Institutional Review Board of Northwell Health immediately, in accordance with policies. All other AEs and problems will be reported at the time of the annual IRB review

Fitbit Wear: 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) or soreness, tingling, numbness, burning or stiffness in hands or wrists from wearing the Fitbit, particularly if the Fitbit wrist band is too tight, which occurs among a small proportion of users. Participants will be instructed via the consent form on methods to reduce irritation (e.g. keep the band clean and dry) and/or hand or wrist senstations (e.g. wear band loosely) and that they can remove the band for a short period of time or stop wearing and contact the study team if the methods outlined in the consent form do not resolve the issue

Loss of Confidentiality or Privacy

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. To ensure confidentiality, all data containing personal identifiers, and used to track contact with patients, will be kept in a secure, password-protected, encrypted Northwell-approved database. No paper documents with personal identifiers will be kept. The PI will be responsible for ensuring that the confidentiality of the data is maintained at all times. All data will be obtained specifically for research purposes.

Personal or identifiable information is not stored on any of the devices used in this study. No information about the participants or the participants' health history will

be shared with Fitbit, except for the information the participants directly share themselves as per Google and Fitbit Terms of Service and Privacy Policies outlined in the consent form.There is no additional risk with using Fitbit as part of this research study as compared to using the device as a consumer.

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.*

Should a participant experience an adverse event, they will be advised to contact their primary care provider. The PI, Dr. Crusco and the IRB will be notified according to established timelines. Should a participant report emotional distress in responding to survey questions, the research coordinators will refer to our Principal Investigator (a licensed clinical psychologist), who will recommend follow-up.

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*

There are no known direct benefits for participating in this study. It is possible that participation may result in increased low-intensity walking and decreased sedentary time, both of which convey benefits to the participant's overall cardiovascular health.

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).*

Names and email addresses from potential study participants will not be collected until participants have read through web information explaining the research study

and protocol and indicated their interest in the study. This information will be stored in a Northwell-approved database store PHI, and it will only be accessible to research staff listed on the approved IRB protocol. Names or other identifying information will not be shared with those outside the research team. Phone numbers and email will only be used for study-related communications, and individuals will only be contacted outside the study if they indicate interest in participating in a future study at the Institute of Health Systems Science.

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 and platforms 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.*

Participants will receive $100 at the completion of the intervention (Month 3) and $150 for successful study completion (Month 6). Additionally, they will be able to keep their FitBit, valued at approximately $150. Participants in the study follow-up period (Months 4-6) may be eligible for a random, weekly lottery of $100 should they maintain adherence to Fitbit activity watch wear and responses to texts messages and surveys.

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.*

Consent and written authorization will be obtained electronically via the 21 CFR 11-approved RedCap platform, with a copy of the electronically signed form emailed to the participants. Before receiving a copy of the consent form, potential participants will be sent through a series of web pages that summarize the study, as well as collect pre-screening information with written authorization.

If a potential participant is deemed ineligible, or if the potential participant is eligible but needs to be waitlisted due to demand, the consenting coordinator will notify the potential participant via email within 2 business days of the initial completion date of the pre-screen.

If the potential participant is deemed eligible, they will have access to the research team email address which can be used to schedule a phone call to go over study details with a consenting coordinator, and have the opportunity to have any of their questions answered. Or they may proceed to read and electronically sign the consent form. Included in this survey will be a short animated video that explains key aspects of the protocol and consent process. Included in these materials will be contact information to reach a consenting coordinator to answer any additional questions before signing the consent form. In order for the consent form to be signed and submitted successfully, potential participants will need to correctly answer 3 questions about the protocol to demonstrate their understanding. PDF versions of signed consent forms will be maintained electronically on a HIPAA-compliant, Northwell Health-approved share drive, accessible only to members of the research team listed on the IRB protocol. A copy of the consent form and signed signature page will be made available electronically to the potential participant.

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.*

N/A

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*

N/A

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. However, the study will proceed with Spanish language

translations should we have difficulty enrolling a sample with the required representativeness.

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.*

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.

All employees of the health system will be eligible to participate in the study. Potential participants will go through online documents explaining that participation in this research will not impact their employment or standing with Northwell Health. Individuals with a supervisory relationship over an employee will not enroll any individual who reports to them in this study. Employee participation or non-participation in this study will have no bearing on an individual's position at Northwell Health.

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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