Title:
Developing a Positive Psychology Intervention to Promote Health Behaviors in Metabolic Syndrome: Proof-of Concept Trial

NCT03473886

Date: 8/16/2018

PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

Rachel Millstein, Ph.D.

PROTOCOL TITLE

Developing a positive psychology intervention to promote health behaviors in metabolic syndrome: Proof-of concept trial

FUNDING

NIH/NHLBI

VERSION DATE

8.16.2018

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

Specific Aim #1 (Feasibility; primary aim): To assess the feasibility of the PP-MI group-based physical activity intervention and outcome assessments in patients with MetS.

Hypothesis: The PP exercises and MI-based goal-setting sessions will be feasible: most (≥50%) of participants will complete 6/8 exercises/sessions. Furthermore, we will be able to obtain objective physical activity measurement follow-up data from at least 80% of enrolled participants at 8 weeks.

Specific Aim #2 (Acceptability): To assess whether the intervention is acceptable to participants, as measured by ratings provided after each PP and MI exercise.

Hypothesis: The intervention will be acceptable: participants will rate each PP and MI exercise with a mean score of at least 7 out of 10 on ratings of ease of completion and helpfulness.

Specific Aim #3 (Outcomes): To assess whether this preliminary intervention appears to result in improvement of physical activity, related health behaviors (sedentary time, diet quality), and psychological well-being (optimism, positive affect, anxiety, depression).

Hypothesis: The intervention will lead to improvements in physical activity, related health behaviors, optimism and positive affect, and reductions in depression and anxiety at 8 weeks compared to baseline.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Metabolic syndrome (MetS). MetS affects 34% of US adults. MetS is comprised of dyslipidemia, central obesity, impaired glucose metabolism, and elevated blood pressure, which together dramatically increase the risk of chronic diseases like type 2 diabetes (T2D) and cardiovascular disease (CVD). Intervening at this pre-disease state can have major implications for reducing morbidity, mortality, and health care costs. Health behaviors, including physical activity, are critical for reducing the risk of MetS and the development of T2D, CVD, and end-organ consequences. Though intensive lifestyle interventions

can prevent or slow MetS, they have been difficult to sustain or implement broadly. The prevalence of MetS is projected to increase, and effective and sustainable interventions are greatly needed.

Physical activity and MetS. Engaging in regular physical activity has great benefits for patients with MetS. Adherence to physical activity recommendations has been associated with better health and reduced risk of progressing to a chronic disease like T2D and CVD. Despite the clear importance of physical activity for MetS patients, most have difficulty achieving the recommended amounts of activity. Furthermore, interventions designed to increase physical activity adherence have been met with limited success.

Positive psychology (PP). PP is an area of study that aims to boost positive psychological states (e.g., optimism, gratitude, positive affect) through systematic exercises, such as performing kind acts, writing a letter of gratitude, or using a personal strength in a new way. These exercises are easily delivered and completed, generally with high participant liking. In research studies, these interventions have consistently increased well-being and reduced depression. Positive psychological states, such as optimism and positive affect, may play an important role in adherence to physical activity and related health behaviors. Despite this, there has been minimal study of interventions in MetS patients that specifically focus on cultivating positive emotional states and their relationship to physical activity. To address this gap in knowledge, we are proposing a study that will focus on the development of a novel positive psychology (PP) intervention, combined with motivational interviewing (MI), a widely-used health behavior change intervention, that is adapted for patients with MetS.

Motivational interviewing (MI). MI is a patient-centered approach to behavior change that can improve physical activity. It has been used in many settings to help patients increase physical activity and other health behaviors. It focuses on clarifying motivation, addressing ambivalence, and setting achievable goals. MI can be used with patients at any stage of change, from those who are not motivated to become active, to those wishing to maintain activity levels. MI integrates well with other treatments and has been successfully combined with health behavior interventions in medical populations.

Creation of an intervention to increase positive emotions and physical activity in MetS patients. The overall aim of this research project is to develop and test a combined PP-MI behavioral intervention to improve positive emotions and increase physical activity among suboptimally active patients with MetS. The first phase was a qualitative research study to gather interview data on 21 participants' experiences of living with MetS (PHS IRB Protocol #: 2016P002824). From these interviews, we have compiled patient preferences and needs to create the present intervention. Finally, there is evidence that neighborhood walkability features (e.g., sidewalks, crosswalks, safety) leads to more walking. In order to help sustain participants' walking behavior, we will bring the groups on various walking routes around the clinics to assess for walkable features.

In this proof-of-concept study, we will run two 8-week PP-MI groups (n=8 each, n=16 total) for primary care patients with MetS. We will use ratings of feasibility and acceptability for each of the sessions and obtain objective physical activity measures pre- and post- group. We will also obtain questionnaire-based information related to health behavior adherence and psychological and physical health to ensure the feasibility of these methods prior to further testing. Finally, we will gather exit interview data to assess participant liking, utility, and additional needs, to allow us to further refine the intervention. If this proof-of concept data demonstrate feasibility and acceptability, the next step study would include a larger, randomized trial to test the feasibility and impact of the intervention.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site

restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

This non-randomized proof-of-concept study will test a novel PP-MI intervention adapted for patients with MetS. The MGH Charlestown HealthCare Center and MGH Revere HealthCare Center will serve as the sources of participants for the study. Each healthcare center will be the site of one group during this phase of research. We will recruit up to 30 patients with MetS (15 from each site) in order to have n=16 (8 per group) complete the study and provide follow-up data; this is to account for drop outs and loss to follow up.

Inclusion criteria:

- Both of the two MetS components most strongly related to MetS outcomes and most sensitive to lifestyle change:
    - elevated abdominal obesity (waist circumference >102 cm in men or >88 cm in women)
        - If waist circumference is not available, body mass index (BMI) will be used as a surrogate measure based on prior research (BMI ≥29.1 kg/m^2 for men and 27.2 kg/m^2 for women).

      AND
    - elevated blood pressure (systolic ≥130 and/or diastolic ≥85 mm Hg or be on blood pressure medication).
- Plus ≥1 additional MetS component:
    - Serum triglycerides ≥150 mg/dL
    - High-density lipoprotein (HDL) cholesterol <40 mg/dL in men or <50 mg/dL in women
    - Fasting plasma glucose >100mg/dL.

      OR
- Fewer than 3 MetS criteria but with PCP approval

- Suboptimal physical activity defined as ≤150 minutes/week moderate intensity activity, which represents less than national-level recommendations.

Exclusion criteria:

- Inability to speak/read English
- Cognitive deficits impeding ability to participate or provide informed consent (measured by a 6-item screen)
- Illness likely to lead to death in the next 6 months per PCP
- Current treatment for cancer, liver, or renal disease
- Pregnancy
- Documented severe mental illness (e.g., psychosis, suicidality)
- No telephone access
- Inability to be physically active
- Diabetes or known or suggested cardiac disease, given that this is a primary prevention study.

There are no exclusion criteria with respect to ethnicity or socioeconomic status.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

The goals are to assess the feasibility, acceptability, and preliminary impact of this newly developed 8-week PP-MI group-based intervention in two pilot groups. Materials will be further revised based on group feedback.

Measures: Following consent and before beginning the intervention, participants will complete the Life Orientation Test-Revised (LOT-R), Positive and Negative Affect Schedule (PANAS), Hospital Anxiety and Depression Scale (HADS), four subscales of the Neighborhood Environment Walkability Survey – Abbreviated (NEWS-A), Barriers to Being Active Quiz, SOM (State Optimism Measure), Community Healthy Activities Model Program for Seniors (CHAMPS), Medical Outcomes Study Short Form-12 (SF-12), Microscale Audit of Pedestrian Streetscapes-Mini (MAPS-Mini) and two dietary screening measures: fruits and vegetables, and fats. Participants will be asked to complete each of these measures at the end of the 8-week intervention as well.

At the first, middle, and final sessions, height, weight, and blood pressure will be collected.

Objective physical activity measures: Participants will be asked to wear an Actigraph GT3x+ for 1 week at baseline and 1 week at follow-up to assess the feasibility of doing so. Accelerometers such as this one are often considered to be the standard for measuring habitual physical activity. They are pedometer-size devices that attach to a belt and are worn at the waist. Participants will also be given a Fitbit Zip to keep, which they will be asked to wear daily for the duration of the study in order to track their steps.

Baseline chart review data: Medical information about enrolled participants will be obtained from the patients, care providers, and the electronic medical record as required for characterization of our population. This information will include data about medical data related to MetS (e.g., blood sugar, blood pressure, body mass index, triglycerides, cholesterol), current medications, and sociodemographic data (age, gender, race/ethnicity, education, and marital status). This information will help us to ensure that the population we recruit indeed does meet MetS criteria, and is a representative population of patients living with MetS so that the intervention data we are gathering is applicable to the broadest population of patients.

Measurement of psychological outcomes. Before and after the intervention, we will measure optimism, positive affect and other psychological constructs that may potentially be impacted by the PP-MI intervention. Doing so in this study will allow us to evaluate the feasibility using of these scales in this specific patient population.

(a) Dispositional optimism (primary psychological outcome measure) will be measured using the Life Orientation Test-Revised (LOT-R), a well-validated 6-item instrument. Dispositional optimism is the positive psychological state most linked to cardiac outcomes, and the LOT-R has been used to measure optimism in many studies of cardiac patients. Though dispositional optimism theoretically would be stable over time, research suggests that LOT-R scores can change in response to psychological interventions.

(b) Positive affect will be measured using the 10 positive affect items on the Positive and Negative Affect Schedule (PANAS), a well-validated scale used in other intervention trials.

(c) Anxiety and depression will be measured using the Hospital Anxiety and Depression Scale (HADS). This well-validated scale has been used in many studies with medical patients (including our group's studies of heart disease), and has the advantage of having few somatic symptom items that can confound mood/anxiety assessment in medical patients.

(d) Environmental barriers and resources will be assessed using four subscales from the Neighborhood Environment Walkability Scale – Abbreviated (NEWS-A), which measures various aspects of the built environment related to walking. The NEWS-A assesses residents' perception of neighborhood design features related to physical activity, including street connectivity, infrastructure for walking/cycling, neighborhood aesthetics, traffic and crime safety, and neighborhood satisfaction. For this study, we will

ask participants to rate their neighborhood on the following four subscales: places for walking and cycling, aesthetics, traffic hazards, and crime.

(e) Barriers to physical activity will be measured using the Barriers to Being Active Quiz, published by the US Centers for Disease Control and Prevention (CDC). This 21-item measure explores seven main categories of barriers, including lack of time, energy, and resources.

Measurement of quality of life and behavioral outcomes. We will also assess selected behavioral and quality of life outcomes.

(a) HRQoL will be assessed via the Medical Outcomes Study Short Form-12 (SF-12), an instrument which has been used in multiple cardiac studies in the past, including our work. The SF-12 also is a reliable marker of QoL in cardiac patients and has been associated with mortality in this high-risk cohort.

(b) Physical activity will be initially assessed using the well-validated International Physical Activity Questionnaire-Short Form (IPAQ-SF). This scale measures self-reported physical activity in the past 7 days in the domains of vigorous activity, moderate activity, and walking. It has been used widely in many populations, with good reliability and acceptable validity. It will initially be used as a screening tool to ensure that participants are sub-optimally active (<150 minutes of moderate-vigorous physical activity in a typical or past week). It will also be used as a follow-up measure at the end of the program. The secondary physical activity measure will be the Community Healthy Activities Model Program for Seniors (CHAMPS), which was designed for use in older adults and is a checklist of activities completed in the past week. CHAMPS includes strength and flexibility items, which the IPAQ-SF does not, and is designed to detect changes in physical activity among older adults (which most MetS patients are, including most of our participants in the qualitative study). The CHAMPS has 41 items, but we will not include the first 6 items which ask about social activities, rather than physical activities, for a total of 35 questions answered by participants.

(c) Diet will be assessed in two broad categories: fruits and vegetables and percent calories from fat. For fruit and vegetable intake, we will administer the CDC's Behavioral Risk Factor Surveillance System (BRFSS) Fruit and Vegetable Module. This questionnaire consists of six items asking about frequency of eating different types of fruits and vegetables. The National Cancer Institute's Percentage Energy from Fat Screener is a 15-item questionnaire that estimates people's typical percentage of energy derived from eating common fat-containing foods (e.g., butter, cheese, bacon).

Prior to week 1. Before the first session, interested and eligible participants who gave phone consent will be offered times to come to their healthcare center to complete the consent form and the questionnaires in person with the study staff. Participants will be provided an option to complete the questionnaire packet at home if they have time constraints. In either case, HADS will be completed in-person with the study staff present. After a participant completes the HADS, we will review their answers to screen for depression. Participants who wish to enroll at that time will be given a copy of the consent form for their records. The questionnaire that will be excluded will be the IPAQ-SF, which will have already been asked on the phone. Participants will also then be given an Actigraph and instructions to track their baseline physical activity for 1 week prior to starting the study. Participants will be asked to bring back their Actigraphs at the first group session. Upon receiving the Actigraphs, the research assistant will upload the data to check for valid wear time. If participants did not wear it for long enough (>4 days), they will be asked to wear it again for a week and return it at the next session. If there is a scheduling constraint such that an interested and eligible participant is not able to attend the pre-study visit, we will offer the option of completing the consent form, questionnaires, and receiving the Actigraph in an abbreviated 30-minute session immediately prior to the first group visit.

Group sessions: overall. All group sessions will be 90 minutes and held in a group room at the respective Healthcare Centers. The overall structure of each session will be: 30 minutes for positive

psychology exercise review/discussion, 30 minutes for physical activity goal setting, education, and discussion, and 30 minutes for a group walk or indoor exercises in inclement weather.

Week 1 session. Participants will be provided with a treatment manual, with weekly PP exercises and information to teach participants about the importance of physical activity and related health behaviors, and set goals to improve these behaviors.

The PI (who will lead all groups) will then introduce the participants to the PP and goal-setting portions of the intervention. For the PP portion, participants will discuss and be assigned the first exercise, gratitude for positive events, and will be instructed to perform the PP exercise during the next week. Prior to completing the exercise, participants will be asked to rate their current levels of happiness and optimism, using a 10-point Likert scale. Immediately after completing the exercise, participants will rate the ease of exercise completion, overall utility of the exercise, and their current levels of happiness and optimism, all using 10-point Likert scales. We will then introduce the first goal-setting session. The leader will discuss the importance of physical activity in MetS. Participants will be given a Fitbit Zip to keep, which they will use to track the number of steps they take each day, for the duration of the study. We will review instructions for use and set a goal for monitoring their baseline physical activity over the next week. Fitbits will not be used as an outcome measure but as a tool that participants can use to monitor their activity and set goals.

Finally, the last 30 minutes will be spent doing a group walk around the local clinic neighborhood. As this will be the first group walk, we will move at a pace comfortable for all participants.

Remainder of weekly sessions (Weeks 2-8). All participants will be asked to complete 8 weekly PP exercises, set physical activity goals, and attend as many group sessions as they can.

Program Content. All sessions will include (a) a review and discussion of the past week's PP exercise, (b) a discussion of the rationale of the next week's PP exercise using the PP manual, and (c) assignment of the next week's PP exercise. For the goal-setting/MI portion, participants will (a) review their goals and steps from the prior week, (b) discuss techniques for improving physical activity (e.g., monitoring physical activity, taking standing breaks), and (c) set goals for the next week. The exercises and content for both PP and MI will be assigned in the same order for all participants receiving them.

Positive Psychology Exercises. The PP exercises used in this study were selected based on their performance in our pilot research and published literature.

> **Week 1: Gratitude for health.** Participants recall three events, small or large, from the preceding week that were associated with satisfaction, happiness, pride, or other positive states related to their health or exercise.
>
> **Week 2: Capitalizing on goals and health.** Participants identify three positive activities related to their physical activity goals and/or overall health and find ways to capitalize on these activities by sharing or celebrating them in some way.
>
> **Week 3: Perseverance.** Participants will think of a time in the coming week when they want or need to use the skill of perseverance to achieve a health-related goal. They will write about how they used perseverance and any associated positive thoughts or feelings.
>
> **Week 4: Enjoyable and meaningful activities.** Participants choose a personal strength that is important to them and then find a new way to use that strength over the following week.
>
> **Week 5: Using personal strengths.** Participants complete a series of self-selected activities that vary between those that bring immediate boosts in mood and those that are more deeply meaningful.

Week 6: Past successes related to health or exercise. Participants will recall a prior event in which they experienced success, around health or exercise. They write about the event, their contribution to the success, and the positive feelings evoked by recalling it. Finally, they consider how they might use the experience to be successful in the future.

Week 7: The good life. Participants will focus on the skill of optimism as they envision and write about their "good life" or how they want their lives to be in one year, related to health, or other important values.

Week 8: Planning for the future. Participants create a plan for using these whichever of these positive psychology skills they found helpful, in a more regular way as they move forward after this program ends.

Goal-setting. The goal-setting portion of the program aims to provide patients with knowledge about the benefits of physical activity, with some basic information about healthy eating, sleep, and sedentary time. This section will assist them with setting goals to become more active and adherent to these health behaviors. Each session follows the same structure. The leader will: (a) ask participants about their physical activity goals and self-monitoring (tracking), (b) provide education about a physical activity, and (c) set an activity goal for the next week. Physical activity goals will be individualized to the participant, and participants will be encouraged to speak with their treatment team if they have any questions about appropriate goals for physical activity. All sessions will involve tracking participants' progress towards their health behavior goals. Participants who complete their tracking each week will be entered into a weekly raffle to win physical activity-related prizes, such as resistance bands and water bottles. The physical activity educational components will vary from week to week:

Week 1: Introduction to increasing physical activity (moving for better health) and self-monitoring. The leader will review with participants the potential health benefits of physical activity, as well as participants' current physical activity. Participants will receive a Fitbit, learn how to use it, and set a goal of monitoring their physical activity (through steps measured by the Fitbit or other device if they already have one) over the next week.

Week 2: Setting a SMART physical activity goal. Participants will learn about setting goals that are SMART (specific, measurable, attainable, relevant, and time-based) and will be encouraged to set a SMART behavioral goal related to physical activity.

Week 3: Barriers and problem-solving. We will review common barriers to being active and ask participants to think about ways to work around their barriers by problem-solving.

Week 4: Finding new routes. At the mid-point of the group sessions, we will introduce the concept of neighborhood walkability and explore the local clinic neighborhood using the MAPS-Mini walk audit. This is a 15-item survey of environmental features that make places more or less walkable, e.g., sidewalks, cross walks, benches.

Week 5: Using neighborhood and social resources. Participants will be asked to identify local resources that can promote activity, such as a local YMCA, a school track, and equipment that they may already have to be more active, such as household items like lifting cans of soup. Participants will also be asked to think about people and community groups that help them engage in physical activity and how they can use them to work toward their goals. Participants will be given resistance bands during this week, along with instructions for use at home.

Week 6: Reducing sitting time/standing breaks. We will bring awareness to the negative effects of prolonged sitting and introduce ways that participants can add in standing breaks to their day, such as standing during TV commercial breaks, and walking during lunch time.

Week 7: Strength training. This session will emphasize the importance of strength training (at appropriate levels) for metabolic syndrome benefit. Participants will be shown additional exercises and ways to do more simple strength exercises at home. During this session, we will also give participants the follow-up Actigraph accelerometer to wear for one week and return at the next session.

Week 8: Managing slips and planning for the future. This session will review ways to keep going with activity even if they have not been progressing as planned. We will review their progress over the past 8 weeks, set short- and long-term physical activity goals, and help participants plan to stay active after the program ends.

Follow-up surveys and Actigraph collection (Week 8). Immediately after the week 8 session, we will distribute the same self-report questionnaires that were administered at baseline (before week 1). These scales should take approximately 30-40 minutes to complete. If participants would rather complete the follow-up questionnaires at home, they may send them back in a pre-paid envelope. We will collect the Actigraphs at this point and upload the data to assess for valid wear time. If participants have not worn them for enough time (>4 days), we will send it home with them and ask them to re-wear it and mail it back. Participants will be mailed a $25 check at baseline and follow-up (up to $50 in total) for completing both the questionnaire packet and returning the Actigraph.

Table 1. Schedule of study events.

	Pre-enroll-ment	Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
Chart review to confirm eligibility	X									
Assessment of inclusion criteria (cognitive screen, low physical activity on IPAQ-SF) and self-reported medical conditions	X									
Chart review for baseline characteristics		X								
Measure weight, height, BP			X			X				X
PP exercise			X	X	X	X	X	X	X	X
MI goal-setting exercise			X	X	X	X	X	X	X	X
Neighborhood walk audit (MAPS-Mini)						X				
Exercise ease and utility ratings			X	X	X	X	X	X	X	X
Self-report measures (LOT-R, PANAS, HADS, BBAQ, NEWS-A, CHAMPS, diet screeners, SF-12, IPAQ-SF, SOM)		X								X
Objective physical activity measurement data (ActiGraph)		X								X

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

This study is in addition to the standard of care at Partners. Programs to help people increase their physical activity are not currently part of the Partners standard of care. All participants will continue to see their PCPs and complete all standard/recommended treatments while they are enrolled in this study. Patients' physicians can refer them to receive counseling to help with physical activity, mental health, or

other aspects of their treatment plan. Patients can discuss these options with their doctors at any time, and they can still be in this study if they choose to also take advantage of those other treatment options.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

Study staff will take all measures to ensure participants' comfort, which includes postponing or ending the questionnaires or exercises at a participant's request. The principal investigator (PI) or other physician study staff will be available to intervene if needed (due to patient discomfort or in case of physical emergency) during all study visits.

As with any study, there is the risk of a breach of confidentiality. These risks will be minimized by using participant ID numbers rather than identifying personal data on study documents. We will also use locked cabinets and locked offices to store physical data. Electronic data (i.e., personal information; step counter data) will be stored in password-protected databases on a Partners computer in a locked office.

In addition, participants may end their participation in the study at any time, for any reason. If they feel their participation is becoming too burdensome or is exacerbating symptoms, they always have the option to decline further participation.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

Medical & psychiatric emergencies. If patients report or study staff witnesses acute medical symptoms, they will be directed to emergency medical care, and their primary medical physicians may be contacted as needed. If study staff have questions regarding medical symptoms and their urgency, Drs. Huffman or Thorndike (MD co-investigators) and the PI will be available to consult as needed.

The main psychosocial safety concern related to patients in this study is regarding depression and suicidal ideation, since we will be asking about depressive symptoms via the HADS. Due to this possibility, the HADS will be administered in person, when the PI, a licensed clinical psychologist, is available to assess and intervene as needed. Though the HADS does not specifically ask about suicidality, if a participant reports suicidal ideation, the PI will complete a suicide risk assessment (see suicide protocol) to assess immediate risk of self-harm or if additional information is needed to clarify risk. If the patient is at imminent risk, the PI will take all needed steps to ensure emergent evaluation, which may include ensuring evaluation in the nearest emergency room. Participants will be informed of these measures to ensure confidentiality—and the limits of confidentiality, such as arranging for emergent medical or psychiatric care if safety is at imminent risk—as part of the informed consent process.

For participants in this study who have elevated depression symptoms as demonstrated by the HADS, we will offer to inform their clinicians and help to facilitate a mental health evaluation as appropriate. For participants who decline enrollment in this study, if the subject is actively suicidal, the study team will intervene to get the patient emergent care via security/ED referral as needed. We have done this in the past in other studies and have established a viable safety plan.

Given that this is a medical rather than a psychiatric population we anticipate the rate of suicidality in this population will be low.

We will ask participants to report adverse events they may have experienced at any time throughout the study. Any adverse events will be reported to the PI and to the IRB according to Partners HRC guidelines, and any events requiring immediate clinical follow-up will be addressed by study physician staff by directly contacting participants.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

Participants may experience discomfort from discussing psychological experiences and could experience the questionnaires as intrusive. Participants who do not find the study to provide a benefit to them may find this upsetting as well. Activities to obtain data through the follow-up assessments may be inconvenient for subjects. We will take all measures to ensure patient comfort and will postpone or end interviews at subjects' requests. We will also ensure that the PI is available to intervene if needed (due to patient discomfort or to answer specific questions about the study), during all study interactions. We have used the briefest methods necessary to assess emotional states and other outcomes to reduce patient discomfort.

All participants will be contacted only after receiving physician approval. Group walks and indoor activities will be conducted at a moderate intensity. Nonetheless, if a participant experiences any physical symptoms during a group walk or exercise, study staff will immediately inform them to stop and sit down, and we will call for emergency assistance. Activities will be performed at or near the primary care clinics, which will also be an available resource for accessing emergency care.

All data will be encoded only with the study participant number that is linked to personal identifying information only in the study database.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

Participants may or may not receive benefit from participation. Participants will complete a series of exercises that are designed to increase optimism, improve well-being, and improve physical activity. Physical activity itself can have important physiological benefits for each of the MetS components. They will be given the opportunity to identify positive emotions and strategies to enhance their own positive emotions. Analyses of PP studies have shown that these types of interventions are associated with improved psychological well-being and decreased depressive symptoms. Optimism and other positive affective states are prospectively associated with increased participation in healthy behaviors and with superior health outcomes. Furthermore, they will have the opportunity to increase and reduce possible barriers to adherence to health-related behaviors. This study has the potential to identify key factors related to poor adherence to health behaviors in MetS patients. Therefore, participants may benefit by seeing improvements in these important and clinically relevant outcomes. Overall, contact with study staff and the follow-up assessments may also provide support and social connection for participants. This may be an improvement over no such contact or systematic evaluation, as is current standard practice.

If the PP-MI intervention in these studies prove to be feasible, well-accepted, and associated with improvements in physical activity and other key outcomes, it may be possible to utilize these easily-delivered and completed exercises as part of a clinical care package for MetS patients. Thus participation in this study may result in benefit to future patients.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

We will recruit up to a total of 30 individuals over age 18 who have at least three MetS risk factors: both elevated abdominal obesity and hypertension, and at least one additional MetS risk factor (elevated blood sugar, triglycerides, or low HDL cholesterol), in keeping with current MetS definitions, or PCP approval or referral. We elected to base inclusion on these MetS risk factors due to i) their demonstrated associations with disease outcomes, ii) that they have shown the largest response to lifestyle treatments, and iii) the feasibility of using the electronic health record to screen for these well-documented factors in primary care notes. Participants must also have suboptimal physical activity adherence (average of less than 150 minutes of moderate-intensity activity per week, representing not meeting national recommendations). This criterion will allow us to assess barriers to physical activity in an already low-active population that has a potential and great need for improvement, while being applicable to a large possible number of MetS patients. This study will focus on increasing physical activity in patients with MetS risk factors because this is a potentially high yield population in a pre-disease state. Intervening with physical activity, one of the most effective health behavior changes patients can make, has the potential to reduce progression to type 2 diabetes, cardiovascular disease, and associated mortality.

The main purpose of our exclusion criteria is to ensure that all potential participants are able to fully participate in the intervention and provide outcome data. Children under age 18 will be excluded because they have a much lower prevalence of MetS risk factors, are not usually directly responsible for their adherence to health behaviors, and they will not be able to provide informed consent. Patients with major medical impairments (e.g., cancer, renal, liver disease) or who have severe mental illness will likely struggle to complete the PP and MI activities, adhere to a plan to increase physical activity, and partake in other study procedures. Pregnant women will be excluded based on potential decreases in their ability to perform moderate to vigorous activity in the later stages of pregnancy, a time when increased physical activity might be contra-indicated. All potential participants will be evaluated for exclusion criteria by their PCP and the principal investigator prior to enrollment.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

For this proof of concept study, we will exclude non-English speaking patients. We do not have study staff who are fluent in Spanish or other non-English languages to conduct the intervention or give the assessments. However, if our overall work in this area does appear to be promising in English, we will plan future studies of the program that do include subjects who speak other languages, since our goal is to develop a program that is applicable and helpful to the broadest set of cultures/languages/people with MetS.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Outpatient recruitment via outpatient clinics. All participants will be adults with at least 3 risk factors for MetS, who are currently under the care of a primary care provider at the two primary care practices that have agreed to be part of this study: MGH Revere or Charlestown HealthCare Centers, or who have fewer than 3 risk factors for MetS who have PCP approval to participate.

Participants will be identified using medical records from these two primary care practices. Once medically eligible patients have been identified, we will confirm eligibility with primary care providers, get provider approval for patient contact, and send potential participants two IRB- approved opt-out letters describing the study (one from the PCP/provider and one from the PI). For patients who do not opt out, we will call them within 2 weeks of mailing the letter to further describe the study (see Recruitment Script) and screen for exclusion criteria. Interested patients will complete the six-item cognitive screener, discussion of medical history to review for exclusion criteria (asking participants to complete the self-report checklist of medical conditions**)**, and complete the IPAQ-SF to ensure suboptimal physical activity.

Outpatient recruitment via Research Patient Database Registry (RPDR). All participants will be adults with at least 3 risk factors for MetS listed in their electronic medical record, or adults with fewer than 3 risk factors for MetS who have PCP approval to participate. Participants can be referred to the study by an outpatient treatment team member (physician, nurse, or nurse practitioner) or through systematic searches using the RPDR at MGH. The RPDR is a centralized clinical data registry that gathers data from various hospital legacy systems and stores it in one place. Researchers access this data using the RPDR online Query Tool. They may query the RPDR data for aggregate totals and, with proper IRB approval, obtain medical record data. The RPDR ensures the security of patient information by controlling and auditing the distribution of patient data within the guidelines of the IRB and with the use of several built-in, automated security measures.
To identify potentially eligible patients:

1.) An RPDR query will be performed to identify those patients with at least 3 risk factors for MetS. Study staff will review the medical record to confirm potential participant eligibility and to identify their linkage to a PCP.
2.) Study staff then will obtain permission for initial contact from each potentially eligible patient's PCP via e-mail or by having providers review letters and discard ones that they do not approve.
3.) For physician-approved patients, study staff will send a study introduction letter signed by the patient's PCP (using secretarial notation or a pdf signature [provider's choice]) and a study opt-out letter signed by Rachel Millstein, PhD (PI). The letter from the PCP informs the patient that he or she is allowing the study to contact patients with at least 3 risk factors for MetS in case they are interested in learning about the trial. Dr. Millstein's PI letter is an opt-out letter describing the study, the procedure to opt out of further contact, and whom to call for further information. These letters will be sent from a central location at MGH.

4.) Should study staff receive no reply within 10 days, staff members will call the patient on the phone to assess interest in the study and to describe the study over the phone. If the patient remains interested, staff will confirm eligibility and assess for exclusion criteria.

Outpatient recruitment via PCPs and flyers. Patients with qualifying risk factors may be referred to this study by their PCPs at either healthcare center. If a potential participant has fewer than 3 of 5 MetS symptoms but has PCP approval or referral, they will also be eligible. We will also post recruitment flyers at each healthcare center, and interested patients may call to inquire about the study and be screened over the phone. If participants screen in and have not been previously approved by their PCP, the study staff will obtain physician approval prior to sending the consent form. If recruitment via PCP referrals and posted flyers is slow, we will (with clinic permission) set up a recruitment table at the clinics with our study recruitment flyer and speak to any interested people. We will not initiate contact nor approach patients. We will only collect the names and phone numbers of those who approached us after having randomly viewed our displayed flyers and are willing to learn more about our research study. Procedures to follow up from this type of recruitment will be identical to those who respond to flyers: e.g., calling them to complete screening questionnaires, obtaining PCP approval.

For all recruitment methods, if a patient remains interested and screens in on the phone, we will mail them a letter with information to invite them to their clinic at a pre-determined time to review the IRB-approved consent form. A study staff member will review it with them, and if they still wish to participate, to sign and keep one copy for their records.

Sociodemographic and medical data (age, gender, education, marital status, medical and psychiatric diagnoses, and smoking history) will be obtained through chart review.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Participants will receive a $25 check after completing each assessment: the initial assessment, which includes the baseline (pre-week 1) questionnaires and returning the Actigraph with sufficient wear-time data, as well as the follow up (post week 8) questionnaires and sufficient Actigraph data. Participants may therefore earn up to $50. After completing the assessment(s), the check(s) will be mailed to participants. We will ask the participants to verify their correct mailing address before the initial session. Participants will also be receiving a Fitbit Zip (retail price $60) and may win raffle prizes of small financial value (e.g., a water bottle, approximately $10).

The study should not result in any additional expenses, and it will not involve extra hospital visits, travel, or other activities that would require out-of-pocket expenses.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

On the recruitment phone call, if the patient is interested in the study after the discussion and screening for exclusion criteria, the PI or research assistant will discuss the study in detail and mail the pre-study visit invitation letter, which reviews the study details and information on where to meet.

If the person wishes to attend the pre-study visit, at that time, study staff will review with them IRB-approved consent form and ask any questions. Interested participants can sign the consent form at this visit. If so, we will give them the questionnaires as described above, and the Actigraph. After this time, research staff will perform a focused review of the subject's medical record (including current medications and laboratory data).

Patients will be informed that they will receive a $25 check for completing each of the assessments.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

All source data (e.g., chart review data and participant self-report) will be entered into the REDCap database. The PI will review this data after each assessment timepoint to ensure that it is being entered correctly and completely.

Safety monitoring will be performed by Dr. Millstein (PI), who will ensure that the study team is adequately identifying, reviewing, and reporting adverse events and unanticipated problems to the Partners Institutional Review Board (IRB). Upon IRB approval of this protocol, we will submit this document to the NHLBI Grants Management Officer prior to beginning any study procedures. Dr. Millstein will also submit an annual progress report confirming adherence to the data and safety monitoring plan, including a summary of any data and safety monitoring issues that occurred since the previous reporting period, as well as any changes made to the protocol and any new and continuing IRB approvals since the last filed report. A more detailed description of monitoring mechanisms, intervals, and the information monitored is outlined below.

Monitoring mechanism: The PI will take primary responsibility for the data safety monitoring. Monitoring will occur on an ongoing basis by the PI, using an Adverse Event log. A committee of mentors will assist the PI as an internal data and safety monitoring team in the event of questions around adverse events. This committee will include Dr. Jeff Huffman (psychiatry, primary mentor), Dr. Elyse Park (psychology, co-mentor), and Dr. Anne Thorndike (internal medicine, co-mentor).

Monitoring intervals: Monitoring of adverse events will occur on an ongoing basis by Dr. Millstein and the research assistant. More systematic weekly meetings for review of feasibility/acceptability information and minor IRB deviations will be held between Dr. Millstein and study staff, including the lead research coordinator. Dr. Millstein will then discuss any potential issues regarding data safety or protocol deviations with Dr. Huffman during weekly supervision meetings. This method will allow the team to review this information and make adjustments to procedures as required. These ongoing, weekly, and bi-monthly reviews ensure that the study procedures minimize research-related risk by reviewing specific outcomes linked to the project. The PI is responsible for directly reporting any serious study-related adverse events to the NIH/NHLBI.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

We will follow all PHRC guidelines with respect to reporting unanticipated problems, including adverse events. Specifically, when a serious or nonserious adverse event occurs, the PI will review the event to determine if it was possibly or definitely related to participation in the research. For all unanticipated problems and adverse events deemed related or possibly related to the research, we will complete and submit an Other Event report through Insight/eIRB as soon as possible and within 5 working days/7 calendar days (as defined in the March 2014 Reporting Unanticipated Problems Including Adverse Events report). At Continuing Review, we will provide a summary of all unanticipated problems

as per PHRC protocol. Finally, if there are unanticipated problems, especially if serious or recurrent, the PI will amend the protocol if it is deemed necessary to protect the safety and welfare of the participants.

Dr. Millstein (study PI) is responsible for directly reporting serious study-related adverse events to the NIH/NHLBI. If there are no such events, a yearly report summarizing adherence to the DSMP, review of study-related enrollment and issues during the study period, and any relevant changes to the protocol, will be sent to the sponsor, NHLBI.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

This study is a proof-of-concept trial to determine if all aspects of the protocol are feasible, acceptable, and effective. After one group (n=8) of participants have completed the trial, we will briefly review the study and our outcomes. If participants' acceptability scores in the PP group are low, optimism scores decrease following the exercises, or we hear that some participants have been dissatisfied with the program, we will alter the protocol to address these issues. Similarly, if our rates of session completion are far below expected rates, we will reassess our protocol and make improvements. We will then complete the more formal data analysis once the second group of (n=8) participants complete the trial. We will seek IRB approval prior to making any significant changes to study procedures if they seem warranted.

On a weekly basis, the research team will meet to review study progress. At that time, the principal investigator will review informed consent documents, study forms, and procedures completed that week, as well as all chart review forms performed that week for completeness and accuracy. The study team will also discuss any procedural difficulties, recruitment issues, and adverse events at this meeting (and before if needed). Investigators will also review consent documents and address acute issues in real time throughout the week. We will take several measures to ensure the integrity of data collection/entry/analysis and the fidelity of our intervention.

Information to be monitored: Information to be monitored by the PI and primary mentor will include: (a) an evaluation of the progress of the research study, including assessments of data quality and timeliness and participant recruitment, accrual and retention consistent with plans for diversity and generalizability, (b) a review of study safety data—adverse event (and minor deviation) information—to determine whether the study should continue as originally designed, be changed, or be stopped, (c) review of procedures to maintain participant confidentiality (e.g., storage of identifiable information in locked cabinets, ensuring study databases have no personal identifying information, use of study participant numbers on communications about the study), and (d) an assessment of external factors or relevant information (e.g., developments in the literature, results of related studies, etc.) that may have an impact on the safety of participants or on the ethics of the research study.

Feasibility and acceptability. Descriptive statistics will be used to calculate: (i) proportions to test feasibility, defined as % of sessions completed, and (ii) means and standard deviations to test acceptability, defined as mean ratings of session ease and usefulness. These will be compared to the hypothesized targets of ≥50% of participants completing ≥6/8 sessions with acceptability ratings >7.0/10.

Outcomes. For physical activity (minutes/day of moderate-to-vigorous activity) and all other psychological, behavioral, and physiological outcomes, I will model changes in the outcomes using a mixed effects regression model with a random intercept for each participant, to account for the repeated measures on each participant and missing data. This will allow me to estimate both the change over time in the intervention group as well as between group differences of MAPP versus EUC at 8 and 24 weeks, correcting for multiple comparisons. In addition to tests of statistical significance, which will be exploratory given the sample size, the effect size (Cohen's d) of the intervention will be estimated for each outcome to aid in design of future trials. I will also perform sensitivity analyses to compare within and between-group effects by gender. For all analyses, an intent-to-treat approach will be used to explore between-group differences, and all tests will be considered significant based on a two-tailed alpha level of .05.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

As noted, risks will be minimized by using participant ID numbers rather than identifying personal data on study documents, and by using locked cabinets/offices and password-protected databases to store personal information. Only study staff (the PI, the research assistant entering data) will have any access to personally identifiable information about participants, and such access will be limited only to information necessary to complete study tasks. The data entered into HIPAA-compliant REDCap database will also be identified only with a number (with this number linked to identifying information that is kept in a separate password-protected database) will be accessed on Partners' secure network.

All data regarding the objective physical activity monitoring devices (Actigraphs) will be encoded only with the participant ID number. The devices will not be marked with any personally identifiable information, and the database that will be used to monitor accelerometer data will only contain participant ID numbers. The accelerometers do not record or link participants' names with their data, and accelerometer data will only be accessed from a locked Partners laptop stored in our locked offices or used on-site in the clinics.

We will ask for participants' email addresses in order to send them weekly reminder emails about session content and dates/times. We will begin by sending emails using the "send secure" encrypted

method. For participants who prefer to receive unencrypted emails, we will review with them the risks of this method, and if they continue to prefer this, we will document this on their contact information sheet and send emails with the PHS-approved disclaimer from that time forward.

"The Partners standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Partners HealthCare. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Partners HealthCare will not be held responsible. Your preference to receive unencrypted email will apply to emails sent to you from research staff in this study ONLY. If you wish to communicate with other research staff at Partners regarding additional studies, your preference will have to be documented with each research group."

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

N/A

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

N/A

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

N/A