Protocol and Statical Analysis Plan

Title: Pragmatic Research in Healthcare Settings to Improve Diabetes and Obesity Prevention and Care for our program MAINTAIN PRIME (Promoting Real (World) IMplEmentation through care teams).

NCT04420936
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MAINTAIN PRIME

Study Information

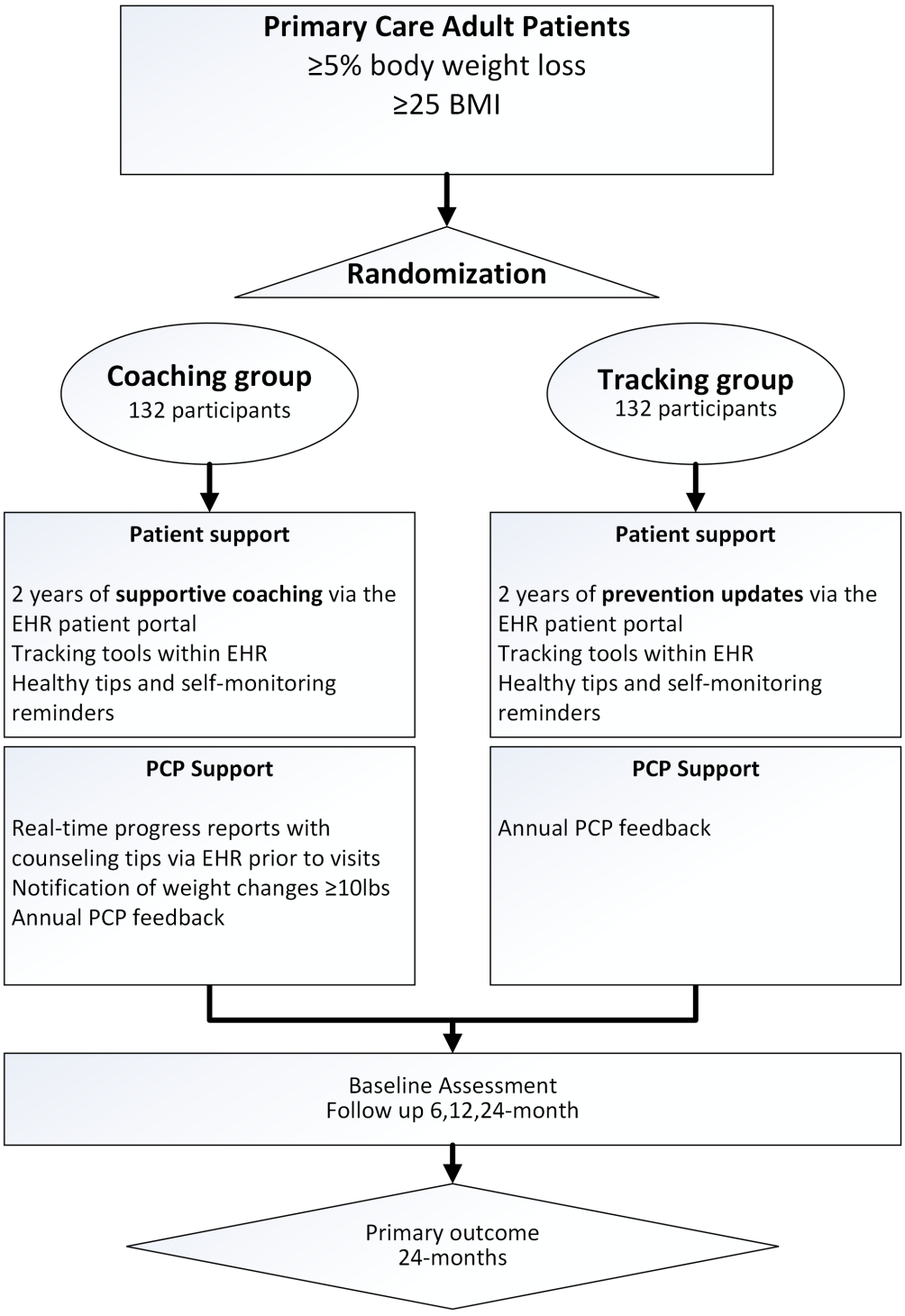
Title	MAINTAIN PRIME (Promoting Real (World) IMplEmentation)
Principal Investigator (s):	Margaret B Conroy (contact), MD, Kensaku Kawamoto, MD
Grant Number:	1R18DK123372-01A1
Funded by:	NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES
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Abbreviations

AE	Adverse Event
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonisation (ICH)
IRB	Institutional Review Board
ITT	Intention-To-Treat
MAINTAIN-pc	Maintaining Activity and Nutrition through Technology-Assisted Innovation in Primary Care
MAINTAIN PRIME	Maintaining Activity and Nutrition through Technology-Assisted Innovation PROMOTING REAL (WORLD) IMPLEMENTATION
NIH	National Institutes of Health
PCP	Primary Care Physician
PI	Principal Investigator
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOA	Schedule of Activities
SOP	Standard Operating Procedures

Study Summary

Title:	MAINTAIN PRIME (Promoting Real (World) IMplEmentation)
Subtitle:	Pragmatic Clinical Trial
Study Description:	MAINTAIN PRIME (Promoting Real (World) IMplEmentation) is a pragmatic clinical trial conducted in 13 primary care practices affiliated with the University of Utah. This study will test the implementation and impact of the MAINTAIN PRIME protocol in routine health care settings.
Objectives:	To capitalize on advances in HIT (e.g., dashboards to track patient populations) and team-based care models to deliver the intervention with minimal support from research staff.
Specific Aim:	Evaluate MAINTAIN PRIME in a pragmatic clinical trial and assess intervention effectiveness after 24 months, with weight change from baseline to 24 months as the primary outcome. Hypothesis. Patients randomized to receive EHR tracking tools and coaching from the primary care team will experience greater weight loss or less weight regain at 24-month follow-up compared to patients with access to tracking tools alone.
Study Design:	This pragmatic randomized controlled trial comparing two EHR-based weight maintenance strategies in the primary care setting.
Endpoints:	24-months
Study Population:	Outpatient adults (BMI ≥ 25 kg/m2) with intentional 5% weight loss in past 2 years
Description of Sites/Facilities Enrolling Participants:	13 University of Utah primary health clinics
Description of Study Intervention:	EHR tools for both groups include weight, diet, and physical activity (PA) tracking flowsheets; standardized surveys; and reminders. Coaching participants will receive 24 months of personalized coaching through EHR patient portal.
Study Duration:	60-Months
Participant Duration:	24-months


Primary Care Adult Patients
≥5% body weight loss
≥25 BMI
Randomization
Coaching group
132 participants
Tracking group
132 participants
Patient support
2 years of supportive coaching via the EHR patient portal
Tracking tools within EHR
Healthy tips and self-monitoring reminders
Patient support
2 years of prevention updates via the EHR patient portal
Tracking tools within EHR
Healthy tips and self-monitoring reminders
PCP Support
Real-time progress reports with counseling tips via EHR prior to visits
Notification of weight changes ≥10lbs
Annual PCP feedback
PCP Support
Annual PCP feedback
Baseline Assessment
Follow up 6,12,24-month
Primary outcome
24-months

Schedule of Activities (SoA): Month +/- 2 weeks

Research Procedures					
	Screening	Baseline	6-months	12-months	24-months
Screening	x				
Consent	x				
Survey Administration	x		x	x	x
Research Measures (In-person visit) Anthropometrics Bloop pressure Recall number steps Recall PA minutes, calories, and fat	x		x	x	x
Randomization & Allocation	x				
Adverse Events		x	x	x	x
Discontinuation of study	x	x	x	x	x

Screening activity, data collection instruments, and responsibility

Screening Procedures			
	Data Collection Instrument	Team Member Responsible	REDCap Instrument Name
BPA, order referral & medical clearance	Epic	Clinic team	N/A
Referral order data collection	REDCap Form		Participant Recruitment Form Primary Care Data Form
Referral order Inclusion confirmation ≥BMI 25 ≥ 5% weight loss Medical clearance Intentional weight loss Ability to perform physical activity English speaker	REDCap Form	Research team	Inclusion Criteria Confirmation Form
Contact documentation	REDCap Form		Initial Contact Log Form
Verbal Consent	Phone call REDCap Survey	Research team	Verbal Consent Documentation
Exclusion confirmation	Phone call REDCap Form	Research team	Eligibility Confirmation Form
Consent	Phone call REDCap Survey	Research team	Intervention Consent Survey
Enrollment, randomization, allocation	REDCap	Study Manager	ENROLLMENT AND ALLOCATION FORM
Decline to further participate	REDCap	Research team	Decline to further participate

Protocol Procedures Schedule					
Research Survey Administration	Data Collection	Baseline	Month 6	Month 12	Month 24
Demographics	Survey	x			
PROMIS	Survey				
Physical function	Survey	x			x
Anxiety	Survey	x			x
Depression	Survey	x			x
Fatigue	Survey	x			x
Sleep disturbance	Survey	x			x
Ability to participate in social activities	Survey	x			x
Pain interference	Survey	x			x
Global Pain	Survey	x			x
PROMIS SF v2.0 - Cognitive Function 4a	Survey	x			x
NIH Toolbox Perceived Stress	Survey	x			x
Physical Activity (BRFSS)	Survey	x			x
Past Medical History	Survey	x			x
Medical history update	Survey		x	x	x
Baseline Weight Maintenance and Behavior Modification Knowledge	Survey	x			x
Mediterranean Diet Score (MDS)	Survey	x	x	x	x
Eating Questionnaire	Survey	x	x	x	x
Patient-Coach Alliance Survey	Survey			x	x
System Usability Scale	Survey			x	x
Primary Care Integration Survey, EHR tools, Net promoter	Survey			x	x
Protocol Activities and Primary Outcome Measure	Survey				
Intervention details video	Survey	x			
In-person research visit I Intervention consult, questions, and concerns (Orientation visit)	In-person session	x			
In-person Patient Research measure	Form				
Height		x	x	x	x
Weight		x	x	x	x
Waist Circumference		x	x	x	x
Blood Pressure		x	x	x	x
Physical activity measured by research accelerometers	Survey	x	x	x	x
Weight loss history	Form	x	x	x	x
Coaching group					
Coaching introduction video	Survey	x			

REDCap instruments for data capture

	REDCap Instrument	Data Entry
Survey Administration		
Demographics	Demographics	Patient
Quality of life	PROMIS CAT v2.0 - Physical Function 4 PROMIS CAT v1.0 - Anxiety 4 PROMIS CAT v1.0 - Depression 4 PROMIS CAT v1.0 - Fatigue 4 PROMIS CAT v1.0 - Sleep Disturbance 4 PROMIS CAT v2.0 - Ability to Participate in Social 4 PROMIS CAT v1.1 - Pain Interference 4 PROMIS - Global Pain PROMIS SF v2.0 - Cognitive Function 4a Perceived Stress	Patient
Medical History	Past Medical History Medical Update Form	Patient
Mediterranean Diet Score	Diet Score Mds	Patient
Physical Activity	Physical Activity Accelerometer Log	Patient
Weight Management & Behavior Modification Knowledge	Baseline Weight Management & Behavior Modification Knowledge	Patient
Eating Behaviors	Tfeiq Eating Questionnaire	Patient
Patient-Coach Alliance Survey	Patient Alliance Survey Coach Alliance Survey Adapted from Coach–Teacher Alliance Validated Questionnaire	Patient Coach
System Usability Scale	System Usability Scale Survey Adapted from System Usability Scale Validated Questionnaire	Patient
Primary Care Integration Survey	Primary Care Integration Survey	Patient
Orientation to study	Intervention Detail Video	Patient
Physical Activity tracker	Accelerometer Log	Patient
Medical Update Form	Medical Update Form	Research Team
Baseline Forms		Research Team
Change in Weigh, Enrollment, and Intention to Participate	Patient Research Measures Form	Research Team
Weight loss efforts	Weight loss history form	Research Team
Patient Goals	Goals Form	Research Team
Randomization and Allocation		
	ENROLLMENT AND ALLOCATION FORM	Study Manager
Study Discontinuation		
Screening phase	Decline to further participate	Research Team
Participant excluded by study team Request to withdraw by participant Lost to follow up	DISCONTINUATION FROM THE STUDY	Study Manger
Pause participation	Snooze From Study From	Research Team
Withdraw	Withdraw from a Research Study	Study Manager
Adverse Events	Adverse Events Form	Study Manger
Death	Death	Study Manager

Operational Procedures Schedule					
Research Survey Administration	Data Collection	Baseline	Month 6	Month 12	Month 24
Physical Activity tracker Accelerometer Assignment Accelerometer Return	Form	x	x	x	x
Participant compensation	Form	x	x	x	x
Appointment for follow-up visit	Form		x		

Procedures		
	REDCap Instrument	Data Entry
Physical Activity tracker	Accelerometer Assignment Form Accelerometer Return Form	Research Team
Participant compensation	Participant Compensation Form	Research Team
Follow-up visit form tracker	Six-Month Appointment Research Visit Form Twelve-Month Appointment Research Visit Form Twenty-four -Month Appointment Research Visit Form	Research Team

Key Roles

- Principal Investigator: Conroy, Kensaku
- RCT Study concept and design: Conroy, Kensaku, Greene, Cedillo
- Statistical analysis: Green, Kukhareva
- Administrative, technical, or material support: Conroy, Kensaku, Cedillo, Zepeda
- Study supervision: Conroy, Kensaku, Cedillo

Grant Team

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Primary outcomes and hypothesis (Specific aim 2 of grant)

Evaluate MAINTAIN PRIME in a pragmatic clinical trial and assess the intervention effectiveness after 24 months, with **weight change** from baseline to 24 months as the primary outcome.

Hypothesis. *Patients randomized to receive Electronic Health Record tracking tools and coaching from primary care team will experience greater weight loss or less weight regain at 24-month follow-up compared to patients with access to tracking tools alone.*

Secondary outcomes

Evaluate MAINTAIN PRIME in a pragmatic clinical trial and assess change from baseline to 24 months for:

Percent change in BMI.
Change in physical activity measured using the self-reported tracking information provided by participants (daily steps, minutes) and accelerometers. Participants will be asked to wear an accelerometer for 2 weeks and then return it by mail.
Change in dietary habits, measured using the self-reported tracking information provided by participants (fat and calories) and validated diet habit surveys and score.
Change in blood pressure.
Improvement in quality of life and function, measured through the General Health, Global Mental, Physical, and Social Health domains from the PROMIS measures that are already routinely collected at many Utah Primary Health Clinics

Study Rationale

A focus on weight maintenance and relapse prevention, increased use of existing staff, and integration with existing Health Information Technology fill a crucial gap in the long-term treatment of obesity as a chronic medical condition.

Background

Obesity is a significant public health problem, and most treatments are short-term. Obesity is a major health problem in the United States and is associated with an increased risk of diabetes. Obesity tends to be a chronic, lifelong condition, and relapse and regain after weight loss is common.[1] Standard behavioral treatment remains the first line of treatment for weight loss [2-5] and includes reduced energy intake, increased energy expenditure, and behavioral treatment, typically delivered in groups.[6] Core

behavioral change strategies are based on social cognitive theory and include goal-setting, self-monitoring, self-efficacy enhancement, and social support.[2, 7-10] Typical weight loss is 8-10% of baseline weight, but results are variable and often fleeting.[11-14] Nearly 20% of participants do not complete weight loss programs, and those who do often regain at least some of the weight lost.[11, 15] At the end of a program, there is generally no sustained access to resources provided during treatment [15, 16] and weight regain is likely to occur.[11, 17, 18]

Weight maintenance interventions are rare, usually not implemented in routine care settings, and lack a plan for sustained use. The proposed intervention will address each of these challenges. Most evidence-based weight management programs have been evaluated in non-clinical settings, and most focus on short-term weight loss rather than long-term weight maintenance. The behavioral principles involved in successful weight maintenance have been examined in a few randomized controlled trials (RCTs).[19-24] However, none of these previous studies integrated with the patient's routine care provided by the primary care provider (PCP) and larger primary care team.

Furthermore, these prior studies have lacked a sustainable model for dissemination and sustained use. We propose to overcome these challenges through a long-term weight maintenance intervention – MAINTAIN PRIME – that is integrated with routine primary care and accompanied by an Implementation Toolkit designed to enable dissemination and sustained use beyond the study. Our approach will also support four features suggested by Rao[25] as being important for an effective weight management intervention: (1) convenient and accessible; (2) lower cost; (3) sustainable participation; and most importantly (4) the ability to retain or re-engage people over several years.

Known Potential Risks

We categorize the frequency of known potential risk using the following categories:

Category	Frequency
Likely	Occurs in >25% of people
Common	Occurs in 10-25% of people
Infrequent	Occurs in 1-10% of people
Rare	Occurs in <1% of people

The expected risks of the study are similar to those experienced in everyday life and involve time and the risk of breach of confidentiality. In addition, in any study, there are expected and unforeseen risks.

The common side effects that we know are:

- Mild discomfort from blood pressure cuff squeezing arm; muscle soreness or fatigue; aggravation of pre-existing muscle, bone, or joint problems (common)
- Increase in anxiety or stigma about being overweight, breach of confidentiality; disclosure of private medical information, exercise–related injury (less common)
- A serious adverse event due to increased physical activity (rare)
- We will notify you promptly about any new study risk if identified

Known Potential Benefits

Participants may or may not benefit from being in this study. Weight loss and physical activity have been linked with improved health and quality of life. It is possible that some may be able to reduce their medication needs (e.g., blood pressure or anti-glycemic agents). Still, there may not be direct benefits to participants. However, the participant will have the satisfaction and the opportunity to help design future systems to improve care.

Potential benefits to society may include better understanding the science of weight management to address obesity and prediabetes in primary care.

Assessment of Potential Risks and Benefits

Minimal risks or discomforts to participants may include breach of confidentiality, lack of privacy, or discomfort due to physical measures (squeezing the arm during blood pressure measurements).

Outcomes and Endpoints

OUTCOMES	ENDPOINTS
Primary	
Change in body weight from baseline/enrollment	24-months
Secondary	
Maintenance of a 5% weight loss	24-months
Change in BMI from baseline/enrollment	24-months
Change in physical activity (minutes and steps per day) from baseline/enrollment	24-months
Change in quality of life from enrollment/baseline (PROMIS)	24-months
Changes in blood pressure from enrollment/baseline	24-months
Change in dietary habits from enrollment/baseline	24-months

OVERAL STUDY DESIGN

Trial design	Pragmatic Randomized Control Trial
Randomization	1:1 to tracking tools with or without coaching
Randomization sequence generation	Stratification by 1) Gender 2) CPG clinic or non-CPG clinic
Allocation sequence	Study manager
Allocation concealment mechanism	After first research visit and confirmation of ≥5% weight loss in the past two years
Blinding	Not blinded

End of Study Definition

A participant is considered to have completed the study if he or she has completed at least one follow-up visit, including the last visit or the last scheduled procedure shown in the Schedule of Activities (SoA).

Inclusion Criteria

Adults aged 18-75
BMI of ≥ 25 prior to this intended weight loss
Have experienced and maintained an intentional weight loss of at least 5% of body weight in the past 24 months
Plan to maintain a University of Utah Health relationship in one of the participating primary care practices
Have or be willing to get an account with the Epic MyChart patient portal embedded in the EHR
Willing to self-weigh at least once a week for the duration of the intervention
Willing to track your food intake at least 3 times per week

Exclusion Criteria

Medical conditions that might cause unintended weight loss such as cancer or thyroid disease
Provider's assessment that patient is unable to safely undertake moderately intense unsupervised physical activity (the equivalent of 30 minutes of brisk walking)
Edematous state that interferes with bodyweight assessment (e.g., severe congestive heart failure, end-stage renal disease, or ascites)
Bariatric surgery in the last 2 years, or planned during the next 3 years
Current or planned pregnancy in the next 3 years
Currently breastfeeding
Perceived lack of basic computer or Internet skills
Unable to attend the orientation/baseline visit or comply with the protocol procedures
Any other underlying reason or concomitant condition, which in the opinion of the principal investigator, could confound the study's results or put the participant at undue risk
Non-English speakers

Consent Summary

MAINTAIN PRIME has a three-step consent process. Details below.

Consent Obtained	Reason	Enrolled by	Methodology	Documentation
Verbal permission	To be contacted by research staff	Providers Clinical Staff	BPA & Study Order	Epic
Verbal Informed Consent	To confirm eligibility criteria	Research Staff	Phone: eligibility confirmation & E-consent	REDCap
Intervention Consent	To participate in study	Research Staff	Phone and REDCap E-Consent Survey	REDCap

Enrollment Summary

Informed consent, a view of the intervention detail video, and weight loss confirmation are needed to complete the enrolment for RCT.
Informed Consent date and signed by participant and research staff consenter
Confirmation of viewing 'Intervention Detail Video' (REDCap Survey)
Weight loss (5%) confirmation at baseline research measure appointment

Retention

Enrolled patients will be tracked in the Epic MAINTAIN PRIME Workbench, which allows to monitor their progress in the trial and run reports on their adherence.

The study multifaceted retention plan consists of the following:
1) Minimizing burdens during protocol design
2) Setting expectations up-front during recruitment and orientation session including weight loss, the demands of joining a randomized controlled trial, and making eating and activity changes
3) Responding promptly to inquiries and messages
4) Sending weekly reminders to track their weight, diet, and exercise through the patient portal
5) Reminders for upcoming visits and tasks

6) Showing appreciation, recognition and accommodating to participant's schedule as much as possible.

In addition, we believe that provider engagement will improve retention. Finally, understanding why a participant chooses to discontinue the intervention will be valuable information to obtain. This feedback may provide insight into what changes can be implemented to improve retention in the future.
Below are additional retention enhancement techniques proven to work by us and other clinical trials (1) that will be integrated throughout the trial's recruitment and retention phases:

- Create 'project identity' that participants can recognize by using similar colors and fonts on trial materials
- Track the eligibility status of potential participants on a computer database
- Write protocols to address common participant questions systematically
- Adhere to trial protocols and procedures
- Provide support to all participants
- Offer flexible scheduling
- Attempt to be on time for clinic appointments
- Make multiple attempts to contact participants for complete data by email, text messages, and phone
- Encourage participants who move from the area to continue completing questionnaires, and have clinic data (e.g., weight, blood pressure) collected and verified by another health professional
- Send birthday cards to all participants

Determine two secondary contacts by asking participants to sign letters notifying contacts of trial participation and giving permission to provide forwarding information (letters also served as an implicit behavioral commitment to complete the trial)

1.Goldberg JH, Kiernan M. Innovative techniques to address retention in a behavioral weight-loss trial. Health Education Research. 2004;20(4):439-47.

Recruitment

Practice-based recruitment

An Electronic Health Record alert, Best Practice Advisory (BPA) functionality available in Epic (UofU Electronic Medical Record system), assists in patient recruitment. The BPA fires and alerts providers about patients in the clinic who meet eligibility criteria (Figure 1).

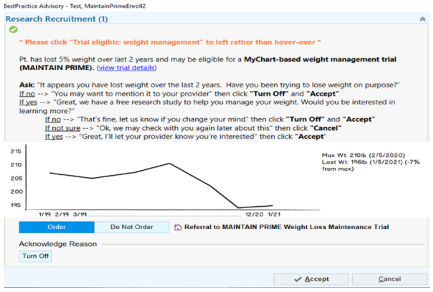


Figure 1. BPA alert for MAINTAIN

The BPA was developed and implemented to send a message/alert to the treating provider and/or his/her medical assistant during the patient encounter to enable these clinical users to inform the patient about the research study and obtain verbal consent of interest to participate and be contacted by the study research team.

Practice-based recruitment is conducted by medical assistants who, after weighing patients, will be prompted by the EHR reminder module to consider referring the patient to the study if study inclusion criteria are met. The prompt includes a script that the medical assistant can use to gauge patient interest and options to snooze the prompt if a patient declines. Clinical providers can also directly refer patients who meet inclusion criteria.

If the patient is willing to be contacted by a research team member to learn more about the study, a study referral option needs to be placed (ACCEPT button in BPA is used to place the order). The user will complete documentation if the patient declines the invitation. When the target recruitment is achieved, the BPA will be stopped. Below a summary of the different recruitment options and details for each option.

Recruitment summary

Recruitment steps	In-person visit with MA	Virtual visit with MA	Virtual visit no MA
BPA Alert	Pop-up BPA notification to MA when weight entered or some other trigger.	Pop-up BPA notification to MA when weight entered or some other trigger.	Storyboard BPA to Provider when Chart Opened.
Permission to be contacted by research team to contact via phone, email, or via the patient portal	MA will tell the patient they may be eligible for a study and ask if they would like to be contacted by the study research team.	MA will tell the patient they may be eligible for a study and ask if they would like to be contacted by the study research team.	Provider will tell the patient they may be eligible for a study, will provide study information and ask if they would like to be contacted by the study research team.
Study Referral Order	If the patient agrees to be contacted, MA queues order for the provider.	If the patient agrees to be contacted, MA queues order for the provider.	If the patient agrees to be contacted, provider places a **referral order**.
	The provider sees unsigned order in the queue, answers questions, and places an order.	The provider sees unsigned order in the queue, answers questions, and places an order.	N/A

RANDOMIZED CONTROL TRIAL INTERVENTION

Study procedures summary

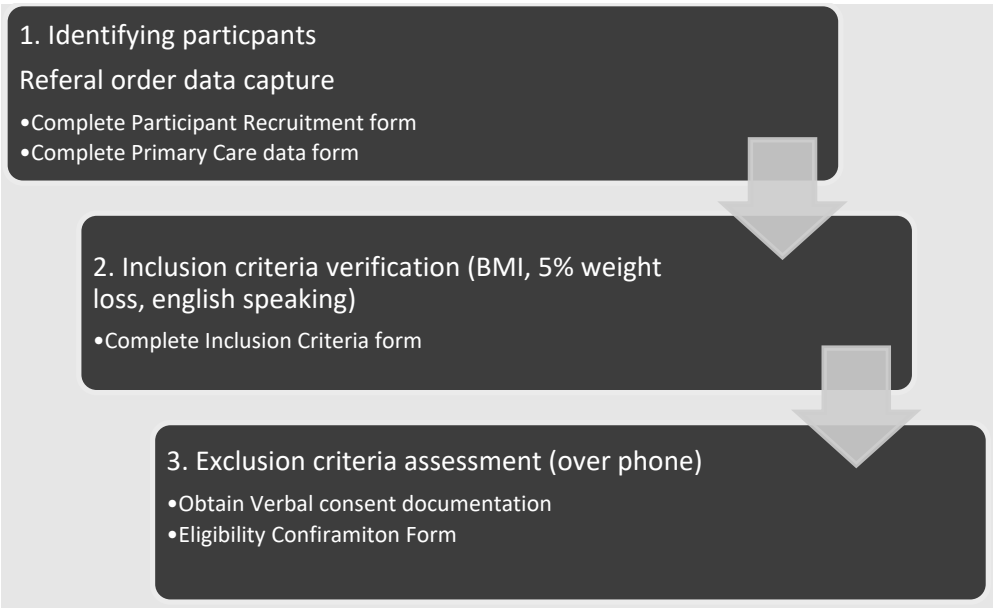


Screening

Objective: Ensure potential participants are eligible to participate

Responsible: Research Study Team

Three-step screening process



Enrollment

Steps	Procedures	Instrument name	Documentation
Identify participants	Identify patients with MAINTAIN PRIME study order placed by running MAINTAIN PRIME Epic Registry	Workbench	Epic
Referral order data capture	• Start a study research record for patient • Confirm medical clearance • Obtain contact information, preferred contact, primary clinic information, and referring provider	Participant Recruitment Form Primary Care Data Form	REDCap Form
Inclusion criteria verification	Confirm 5% weight loss, a BMI greater than or equal to 25 within the past two years, medical clearance, English speaking, or if a referral order was placed by mistake.	Inclusion criteria confirmation Form	REDCap Form
Eligibility confirmation 1. Verbal consent	• Call participant • Obtain verbal consent to assess eligibility confirmation • Review and completion of the verbal consent document • Send verbal consent via REDCap for participant's records • If the participant doesn't provide consent, **STOP**-- The phone eligibility confirmation cannot be conducted • If not interested and decline to further participate, document reasons using the decline to further participate form	Verbal Consent Documentation Decline to further participate	REDCap Survey REDCap Form
2. Confirm eligibility via phone call survey	• If participants provide verbal consent, CONTINUE the phone eligibility confirmation. • If not a good time to talk, schedule a callback appointment using the Initial Contact Log form • Confirm additional inclusion/exclusion criteria • Schedule research measure baseline visit	Eligibility Confirmation	REDCap Form REDCap Calendar & MAINTAIN PRIME Outlook Calendar or Microsoft Booking
3. Confirm maintenance of weight loss with baseline research measures	• Confirm participant's current weight is ≥5% of maximum weight (Weight Goal 5%) • If weight loss 5% confirmed, then eligibility is confirmed	Research Measures Form	REDCap Form
Screen Failure	• Notify participant and document in REDCap as protocol violation, screen failure ○ Code 0= Unable to maintain 5% weight loss at baseline using weight (kg) research measure • Inform participant of the screen failure policy found below. • Provide Dr. Conroy's contact information if further information is needed	Participant Discontinuation Form	REDCap Form
4. Randomize, Enroll, and Allocate	The research team notifies the Research Study Manager to run randomization and allocation.	Enrollment and Allocation Form	REDCap Form

Screening Failures

- During the eligibility confirmation phase, individuals who **do not meet the criteria** for participation in this trial will be told why they cannot participate by the research staff.

- Should the participants be willing, they may come back for a rescreening visit (also the baseline measure) if they meet the entry criteria at a later date during the study's recruitment phase.

- Rescreened participants should be assigned the same participant number (study ID, SID) as for the initial screening.

Informed Consenting Procedures and Documentation

- The 'consenter' is any listed investigator or designated research team member that can obtain informed consent from the participant before the start of any research procedures.
- Research members review Epic MAINTAIN PRIME Workbench referrals and contact the patient to confirm eligibility via verbal consent, answer any patient's questions, and confirm an active MyChart account.
- If the patient agrees to participate:
    - The patient is then consented and emailed an e-consent via REDCap or mailed a consent by the research team.
    - Upon receipt of signed informed consent, the patient is scheduled for a baseline research visit by the research team.

Steps	Procedures	Instrument name	Documentation
Review consent document	Explain study Answer patient questions	Informed Consent Documentation	REDCap Survey
Consent document	Send consent for patient signature Scheduled baseline research measure	Informed Consent Documentation	REDCap Survey
	Consenter must sign and date the consent document stating consent form has been reviewed and questions and concerns addressed	Informed Consent Documentation	REDCap Survey

- Consent documents without the consenter's signature are invalid documents and participants will NOT be able to continue their participation in the study

Baseline assessment and research activities

Please refer to the Schedule of Activities (SoA) for a complete list of baseline questionnaires, activities, and measures.

Baseline Research Activities	
ACTIVITIES	METHODS AND DETAILS
Research baseline surveys	Will be sent using automated invitation function in REDCap after informed consent signature.
Reminders for research baseline survey completion	• Reminders for completion of baseline questionnaires will be sent automatically and can be adjusted manually in REDCap. • Reminders are set up every 2 days for up to 5 reminders per research survey.
Intervention details presentation video	• Will be sent via REDCap survey. • The intervention details video will cover the skills needed to continue with the healthy behaviors that are key for weight management. • The content also includes basic nutrition concepts, including eating a well-balanced diet, self-monitoring calories and fat to enable weight maintenance, increasing spontaneous and planned physical activity, and behavior modification problem solving, goal setting, and relapse prevention skills. • Participants will be asked to confirm viewing the entire presentation video.
In-Person Baseline Research	In person visit, 1:1 Participant and research member
Program clarification	Research member will review key concepts of intervention details presented in videos.
Goals	• Research member will provide goals for calories, grams of fat, minutes of physical activity, and steps according to participant's individual progress and weight management phase. • Research member will review participant's goals and MyPlate Meal Plan in detail with the participant. • Documentation of goals is done via REDCap using the 'Goal' instrument. • A printout of the Goal Form and MyPlate Meal Plan can be provided to participant.
Research measures	Research member will obtain research measurements for weight, height, blood pressure and waist circumference. Please refer to Appendix 1.
Other Resources provided	Participants will receive a pedometer, food, or weight scale if needed.
Accelerometer	Accelerometer assignment and demonstration.
Resources	Participants will be provided handouts or weblinks of intervention components as needed.
Follow-up Research Visits Schedule	• Participants will be scheduled for all upcoming research visits and given a printed schedule. A phone call and/or text reminder will be sent out 1 week before the study visit. • Patients will be asked to confirm visit or reschedule OR • Participants will receive a self-booking invitation via Microsoft Bookings and REDCap- Reminders for self-booking are set up every 2 days for up to 5 reminders.
Coaching Video*	A coaching video will be sent to the **coaching group.** The content includes information on the coach's role and the use of MyChart to communicate with the coach. Explanation of the brief assessment questionnaires relevant to weight management topics (e.g., well-balanced diet assessment, physical activity assessment, self-monitoring assessment, etc.), including a text field to discuss questions or challenges with the coach, will be covered.

* Coaching group only

Randomization and allocation

After completing the baseline assessment participants will be randomized to participate in either the coaching or tracking group intervention (132 individuals will be randomized to each group).

Blinding

Not blinded.

Follow up intervention procedures

Please refer to Schedule of Activities (SoA), for a complete list of follow-up questionnaires and activities.

For coaching group:

After the baseline research visit and allocation of the intervention group, research members will assign a coach to the participant and be assigned questionnaire series, goals, tracking sheets, and status participation via Epic by the research team.

Intervention Activities for the coaching group

Follow-up Research Procedures	
Epic instrument name	Assignment
MAINTAIN PRIME Flowsheets Status	Status in study Group assigned (coaching or tracking group) MAINTAIN PRIME Coach
MAINTAIN PRIME Flowsheet goals	Calories, Grams of fat, Physical Activity Minutes, and Steps
MAINTAIN PRIME Questionnaire Series	Assign Questionnaire Series to participant Send Orientation Questionnaire (first assessment questionnaire)
MYCHART MAINTAIN PRIME weight exercise flowsheet	Assign tracking log to participant

Research members' additional contacts throughout the study include letters, phone calls, emails, newsletters, postcard, texts, patient portal, and reminders as needed.

*Please refer to Epic system procedure for research team SOP for details.

Follow-Up Intervention Procedures for participants						
INTERVENTION ACTIVIITES	COACHING [1]	TRACKING [2]	Month 1	Month 2-6	Month 7-12	Month 13-24
Complete assessment questionnaires via MyChart	x	Unrelated to weight maintenance	Weekly	Biweekly	Monthly	Quarterly
Receive feedback from coach	x		x	x	x	x
Complete additional questionnaires, if necessary	x		x	x	x	x
Track weight, physical activity minutes, steps, and calories/fat in MyChart	x	x	x	x	x	x
Receive reminders to log into MyChart	x	x				
Communicate with coach via MyChart	x					
Make regular PCP appointments	x	x	x	x	x	x
Wear accelerometer for 2-weeks at end of	x	x	Month-0	Month-6	Month-12	Month-24
Have PCP receive regular summary reports, in an Epic note format, on progress after research visit created by research team	x	x		Month-6	Month-12	Month-24
Real time progress reports automatically generated in Epic	x		Before routine schedules			
Weight change notification when +/- 10 lbs.	PRN					
Receive encouragement to follow-up with their PCP on a routine basis.	x	x				
Learn that their PCP may choose to discuss the data they receive through MyChart as a part of their routine medical care.	x	x				

[1] Coaching Group
[2] Tracking Group

Final evaluation

- Please refer to Schedule of Activities (SoA) for complete list of endpoint questionnaires and activities.

Study intervention fidelity

Intervention fidelity will be monitored regularly, both electronically and through a 10% random sample chart audit by the study manager quarterly. Deviations from the intervention protocol will be promptly addressed with the health coach. For each coaching note, coaching quality will be assessed using a 1 (very poor) to 5 (very good) scale. Missing notes will be automatically given a 0.

PARTICIPANT DISCONTINUATION OR WITHDRAWAL FROM STUDY

Discontinuation of study intervention

- Participants may withdraw voluntarily from the study, or the PI may discontinue a participant from the study.
- Participants who sign the informed consent form, are randomized, but do not receive the study intervention may be replaced.
- Participants who sign the informed consent form, are randomized, and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

Epic documentation of discontinuation of study intervention is done by updating the status of participant in the MAINTAIN PRIME Study Flowsheet and REDCap instrument- Withdraw from a Research Study

Discontinuation of study intervention will be documented using REDCap instrument- Discontinuation from the Study

Data Use

For participants who **have formally withdrawn**, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

For participants who have a protocol violation:

For participants who are lost to follow up (unable to contact/schedule but had **not** formally withdrawn), EHR weights might be used if available.

Categories for participant discontinuation from the study

Discontinuation categories:

- Decline to further participate, before consenting participation
- Screen Failure, after consenting but unable to maintain 5% weight loss at baseline visit determined by using the weight (kg) research measure
- Withdraw by participant: Participants are free to withdraw from participation in the study at any time upon request. Withdraw from intervention (treatment) doesn't exclude the participant from continuing to provide research measures (with research or clinic staff) if agreed to.
- Lost to follow up: Please refer to section below.
- Protocol Violation: An investigator may discontinue a participant from the study for the following reasons:

Protocol Violation Reason	Details	Category	Documentation
Screen Failure	Unable to maintain 5% weight loss at **baseline** using weight (kg) research measure	Protocol Violation*	REDCap Discontinuation Form and Allocation Form (enrollment status = screen failure)
Participant's safety	Primary care provider feels that it is not in the participants best interest to stay in the study	Protocol Violation	REDCap Discontinuation Form
Change in health condition	Pregnancy or other disease or condition that is part of the exclusion criteria of the study	Protocol Violation	REDCap Discontinuation Form
Confounding condition	Underlying or concomitant condition, which in the opinion of the principal investigator, could confound the results of the study or put the participant at undue risk	Protocol Violation	REDCap Discontinuation Form
Study stopped	Study can no longer provide intervention	Protocol Violation	REDCap Discontinuation Form

Lost to Follow-Up

The following actions must be taken if a participant fails to return to the research office for a required research measure visit (documented in the REDCap calendar as NO SHOW):

- Contact the participant and reschedule the missed visit within 24 hours
- Counsel the participant on the importance of maintaining the assigned visit schedule
- If unable to contact, send letter, email, or MyChart message addressing the importance of maintaining the assigned visit schedule.
- Provide participant contact to PI for further follow up with participant if indicted.

For participation to be discontinued and documented as lost to follow up, it should meet **all** the following criteria:

Lost to follow up criteria applies ONLY for research measures visits	
ACTION	DETAILS
No show	Participants stop reporting to scheduled research measure visits and cannot be reached to complete all protocol-required study procedures.
Multiple failed attempts to reschedule	The research team complied to attempt to contact the participant and reschedule the missed visit within 24-hours of a missed visit and has not been able to reach participant.
Failed efforts to regain contact	The research team has made every effort to regain contact with the participants.
Attempts to regain contact	2 calls, 2 texts, 2 emails, 1 MyChart message

Efficacy Assessments

Efficacy of the intervention will be assessed primarily through the assessment of body **weight change** from baseline/enrollment to 24 months.

ADVERSE MEDICAL EVENTS

Severity of Event

Participants will be asked about any adverse medical events that might have affected their participation in usual daily activities at each follow-up assessment and self-rate the severity of the event.

For adverse medical events, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities
- **Moderate** – Events result in a low level of inconvenience or concern with intervention measures. Moderate events may cause some interference with functioning
- **Severe** – Events interrupt a participant's usual daily activity. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate too "serious"
- **Life threatening**: Event is serious and explained in detail on Serious Adverse Event (SAE), section.

Relationship to Study Intervention

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

Related – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
Not Related – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.
Please see Appendix I, Table 8 for detailed documentation.

Expectedness

The investigators do not anticipate any adverse events related to this study, but study events will be closely monitored, documented, and reported to IRB as needed.

Adverse Event Reporting

Serious Adverse Event: Serious Adverse Event (SAE): fatal or life-threatening, requires or prolongs hospitalization, produces a persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or based on appropriate medical judgment, may jeopardize the subject's health, and may require medical or surgical intervention.

- Any unexpected adverse events associated with the research that are fatal or life threatening will be reported to the IRB within 24 hours.
- Any unexpected adverse event associated with the study that is moderate to severe, but not life threatening, will be reported to the IRB in 10 days.

STATISTICAL CONSIDERATIONS

Sample Size Determination

Statistical Power of Primary Analysis of Percent Weight Change. Based on an analysis of baseline and 2-year weight data from 157 patients of the MAINTAIN-pc cohort, we estimated a standard deviation in percent weight change to 2 years of 8.8% and a Pearson correlation between the baseline weight and percent weight change of -0.13. Assuming that, loss-to-follow-up does not exceed 25%, 99 evaluable patients in each group (representing 132 randomized patients per group, or 264 total randomized patients) will provide 80% power with 2-sided α=0.05 to detect a mean difference of 3.5% in the percent weight change from baseline to 2 years. The effect size of 3.5% is comparable to that achieved in the original MAINTAIN-pc trial.

General Approach

Statistical power and analysis. General considerations. Data analyses will be performed by the Study Design and Biostatistics Center (SDBC), the statistical core of the Utah Center for Clinical and Translational Science. Three types of analyses will be performed to address Aim 2, which is the Specific Aim that addresses the primary analysis of the clinical trial: 1) Descriptive summaries of baseline factors, 2) Descriptive summaries of adherence for the two randomized groups, and 3) intent-to-treat (ITT) analyses comparing the primary % change in weight outcome and other secondary outcomes between randomized groups. In accordance with the intention-to-treat principle, all ITT analyses will analyze patients in accordance with the randomly assigned treatment, irrespective of compliance. We have designated a single primary comparison of the percent change in weight between the randomized groups at 24 months after randomization. Additional details of the three analysis categories, power calculations, and methods for addressing missing data are provided below.

Descriptive Summaries of Baseline Factors. Standard descriptive statistics (proportions and frequencies for categorical factors; means, standard deviations, and designated percentiles for numeric factors) will display characteristics of enrolled and randomized subjects, overall and by clinical site. Baseline characteristics will also be summarized by randomized treatment group with standardized mean differences to quantify balance in baseline factors between the MAINTAIN PRIME intervention and control groups.

Descriptive summaries of adherence for the two randomized groups. Importantly, all the analyses described below follow the intent-to-treat principle, and thereby provide pragmatic evaluations of effectiveness of assignment to the respective interventions given the levels of adherence achieved by each intervention. Hence, to clarify the interpretation of the ITT comparisons, we will provide numeric tabulations and graphical displays to summarize adherence measures (e.g., days of tracking in EHR

each month) in each randomized group throughout the intervention period. Additional analyses summarizing adherence and process outcomes are described in Aim 3 of the Research Plan.

Intent-to-treat comparisons of outcomes between the randomized groups. Percent change in weight will be compared between the randomized groups using a longitudinal mixed effects model95 which includes the percent changes in weight from baseline at 6 months, 1 year, and 2 year follow-up as the outcome. Fixed effects in the longitudinal model will include baseline weight, randomized treatment group, clinical center, other randomization stratification factors, follow-up visit time (as a categorical factor) as well as interactions of follow-up visit time with each of the other factors in the model. Adjustment for baseline weight will account for any random imbalances in baseline weight and will optimize statistical power as in analysis of covariance (ANCOVA).96 Because there are only four follow-up assessments, an unstructured covariance matrix can be used to account for correlation of serially measured outcomes in the same subject to avoid imposing specific assumptions concerning distributions of random effects.97 The comparison of mean percent weight change at 2 years will constitute the primary evaluation of the effectiveness of the MAINTAIN PRIME intervention. We will also construct linear contrasts to estimate the adjusted mean percent change in weight by randomized group as well as differences in mean percent weight change between the randomized groups at each follow-up time to fully characterize the effectiveness of the MAINTAIN PRIME intervention over time. For each comparison, we will provide point estimates with associated 95% confidence intervals.

ITT analyses of other outcomes. Similar linear mixed effects analyses will be applied to compare quantitative secondary outcomes including the number of steps per day (as a measure of physical activity), composite dietary score (from Rate My Plate), patient reported quality of life (General Health, Global Mental, Physical, and Social Health domains from the PROMIS measures), blood pressure, and patient satisfaction between randomized treatment groups. For outcomes which deviate substantially from normality, and which cannot be readily transformed to approximate normality, we will use generalized estimating equations (GEE) under generalized linear models with outcome models and link functions appropriate to each outcome.98 In particular, GEE for repeated binary outcomes will compare dichotomous outcomes between randomized groups, and GEE for ordered categorical outcomes will compare ordered categorical outcomes.

Missing Data. Rigorous treatment of missing data is particularly important for evaluation of behavioral interventions where loss-to-follow-up can be expected to correlate with the patients' response to treatment. We plan to apply multiple imputation to impute missing outcome data, using comprehensive imputation models that include both non-missing measurements from the variables included in the data analysis as well as additional auxiliary variables that are considered to be predictive either of the risk of missingness or the values of the variables whose missing values are being imputed.99 Imputation of missing weight measurements will account for non-missing weights at other follow-up assessments. Multiple imputation has been established as superior to alternatives including complete case analysis or simplified ad-hoc single imputation approaches.100 We plan to implement multiple imputation by creating 20 independent imputed data sets using fully sequential multiple imputation,101 and applying Rubin's formulae to estimate standard errors for use in hypothesis tests

and confidence intervals. The application of multiple imputation will assure that statistical inferences are approximately unbiased so long as the mechanism of missingness follows a missing at random (MAR) structure after accounting for both the analysis and the auxiliary variables included in the imputation models.102 In further sensitivity analyses, the main imputation models will be extended as described by Moemie et al.23 to evaluate the sensitivity of our results to the possibility that data are missing not at random (MNAR). In missing not at random models, the mean values of outcome measurements are assumed to differ by a designated nonzero amount between missing and non-missing values after accounting for all the other variables in the imputation model. The sensitivity analysis will assess how large this difference must be to alter conclusions.

Regulatory, Ethical, and Study Oversight Considerations

Informed Consent Process

IRB approved consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention.

Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be approved by Institutional Review Board (IRB), and the participant will be asked to read and review the document. The investigator or study staff will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and their rights as research participants.

Participants will have the opportunity to carefully review the written consent form and ask questions before signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it before agreeing to participate. The participant will sign the informed consent document before any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. The participants will be given a copy of the informed consent document for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

All research personnel obtaining consent will have completed the appropriate research compliance education (IRB modules) and will be trained by the project manager on the appropriate consenting procedures set forth by the University of Utah IRB. An investigator will be available by phone if the participants have additional questions or concerns, they would like to discuss before they provide their informed consent, as specified in the informed consent documents.

Study Discontinuation and Closure

This study may be suspended or prematurely terminated if there is sufficient reasonable cause. Written notification (letter signed by PIs), documenting the reason for study suspension or termination, will be provided by the suspending, or terminating party to study participants, investigator, funding agency, and regulatory authorities.

If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Termination, Suspension, and Stopping rules

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency and IRB.

Stopping rules

In this minimal risk healthy lifestyle intervention trial, it is more likely that dropouts and difficulty in recruiting adequate numbers of participants will require stopping the trial than that excess medical adverse events will occur and require stopping the trial. However, as outlined elsewhere, we will monitor injury rates in all participants and the safety officer, together with the study investigators, will alert the IRB and the NIH if a larger than expected injury rate should occur in the treatment group.

Issues or circumstances relating to stopping rules for this trial include:

- Pregnancy: a female of child-bearing age that becomes pregnant will be removed from participating in this study.
- Bariatric Surgery: participant that schedules bariatric surgery during the next two years after study enrollment will be removed from participating in this study.
- New Information: It is exceedingly unlikely that any new information will become available during this trial that would necessitate stopping the trial.
- Limits of Assumptions: It is possible that baseline differences between the groups, excessive study dropouts/or missing data by the interim measurement time point will limit the value of

data analysis of measurements at the 2-year time point. Baseline differences will be evaluated after the first measurement time point and effects on the power to detect differences in the 2 primary outcomes will be evaluated and communicated to the PI, safety officer and NIDDK. Given the monitoring plans outlined elsewhere in this document, it is exceedingly unlikely that there will be baseline differences between groups of any magnitude to threaten the study's validity.

Limits of Rules: Acknowledge that other situations could occur that might warrant stopping the trial and have a section on the safety report entitled 'Other situations that have occurred since the last safety report that warrant discussion' to allow for communication of concerns to the study PI, statistician, and the safety officer.

Dropout rates

Dropout rates higher than 25% would be of concern, so we propose to monitor the dropout rates quarterly. Alert points are set at dropout rates of 20% (low alert), 30% (mid-alert), 40% (high alert) and 50% (extreme alert). With early alerts to problems, action would be taken to avoid higher level alerts; if a higher-level alert should arise, more drastic remedial action would be involved.

The actions taken at each level of alert are given below:
Mid-level alert = Conference call between study investigators to discuss approaches to minimize further losses to follow-up/dropouts
High-level alert = Conference call between investigators to determine further alterations of study protocol to complete the study with no further losses
Extreme-level alert = In the unlikely event of a 50% dropout rate occurring before the 1-year measurement time point, study investigators would convene on a conference call to discuss the usefulness of continuing the study. However, if a 50% dropout rate occurred during the 2nd year of follow-up, it might still be of interest to continue the study; study investigators would convene on a conference call to discuss whether to complete the study.

Confidentiality and Privacy

- After consent is obtained, participants will be assigned a study ID number (SID). Subsequent information will be identified only by this ID number.
- Strict confidentiality of information collected will be maintained.
- All research staff will complete the required research information and training modules.
- Participants access MyChart via a password-protected website or Smart-phone which is hosted on a secure University of Utah server.
- Each authorized participant logs in with an assigned username and secure password. Only then, can they access online lessons and input and information about his or her weight, daily intake of calories or fat, and physical activity.

- An individual can only access his or her information about lifestyle modification.
- The participant can send messages to his or her lifestyle coach via the MyChart messaging system.
- All participant information from the MyChart website, including participant research codes and email addresses, is encrypted.
- The encryption key is stored within the application in a compiled format, not in a database or flat file. Only an authenticated supervisor-level user can create new users on the system, and no deletions or updates are supported through any user interface.
- All paper-based data will be kept in a secure, locked location, accessible only to research staff.
- Electronic data will be kept in a password-protected database that is only accessible to research staff.
- Data confidentiality will be closely supervised.

Future use of data:

- Data collected for this study will be analyzed and stored at the University of Utah Study Design and Biostatistics Center (SDBC).
- Data analyses will be conducted on de-identified data.
- Research records including identifiable data will be securely stored according to the current IRB guidelines.
- Data will be anonymized, and the link destroyed (shredded) after this time.

Data safety and monitoring plan

The safety officer for this trial will by **J. Robinson Singleton, MD**. Dr. Singleton practices clinically as a neurologist, has experience running lifestyle intervention studies, and serves as the Director of the Clinical Trials Support Foundation and Medical Director of the University of Utah Center for Clinical & Translational Science Liaison Team. He is familiar with the medical safety issues that can arise with a lifestyle intervention such as that to be delivered in MAINTAIN PRIME. Dr. Singleton will review the reports sent by the study manager (at the agreed frequency) and will use the checklists in the Appendix Section to this document to determine whether there is any corrective action, trigger of an ad hoc review, or stopping rule violation that should be communicated to the study investigator, the University of Utah IRB, and the NIDDK. Given his expertise in lifestyle trials and leadership roles in clinical trials at the University of Utah, Dr. Singleton will be an invaluable resource to MAINTAIN PRIME.

Measurement and reporting of subject accrual, adherence to inclusion/exclusion criteria

A review of the rate of subject accrual and adherence to inclusion/exclusion criteria will occur weekly during the month recruitment phase. Review will occur at the end of each recruitment wave (every 3

months) of 66 participants (25% of subject enrollment) to assure that participants meet the eligibility criteria and ethnic diversity goals outlined in the grant proposal.

Measurement and reporting of participant compliance to treatment protocol

Once participants randomized to the treatment group have started the intervention, data on compliance to the treatment protocol will be collected automatically via EHR reports and research staff and reviewed quarterly by the study investigator, the study statistician, and the safety officer. If the safety officer has concerns about whether compliance has reached a level that might inhibit the ability of the study to test its primary hypotheses, he/she will suggest a conference call for study investigators to discuss methods for improving compliance. As per the previous Electronic Health Record (EHR)–based coaching intervention (Conroy et al. 2019) data on expected compliance to the proposed protocol, 80% can be used to determine a 'trigger point' for this action.

In addition, we will use clear process evaluation protocols for monitoring the intervention arms to ensure that the integrity of the intervention is maintained. The Intervention Team, made up of Drs. Conroy, Dr. Kawamoto, the project manager, and research assistants will meet weekly throughout the study. These meetings, we will review progress (e.g., participant recruitment, online program use), check record-keeping to make sure it is up to date, and address problems as they arise. We have developed online tools that monitor patient progress and track whether the lifestyle coaches are delivering the virtual intervention per the designated schedule and facilitate auditing online coaching notes (e.g., to check length and content). The co-investigators will provide the staff with feedback based on these intervention audits, and initiate additional training as needed. Compliance on the part of participants will be evaluated according to the study protocol.

Data Collection Responsibilities

Data collection is the responsibility of the clinical trial team at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Study Records Retention

Study documents should be retained for a period of five years from the date of NIH Federal Financial Report (FFR) submission.

Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Hgrouponisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the investigator to use continuous vigilance to identify and report deviations within 5 working days of identification of the protocol deviation, or within 5 working days of the scheduled protocol-required activity. Deviations must be addressed in study source documents, reported to NIH Institute, and Principal Investigators Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements. Further details about handling protocol deviations will be included in the MOP.

Publication and Data Sharing Police

This study will be conducted under the following publication and data sharing policies and regulations: National Institutes of Health (NIH) Public Access Policy ensures that the public has access to the published results of NIH-funded research. t requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. as such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Researchers may request data from this study after completing the primary endpoint publication by contacting Dr. Conroy.

Appendix I

Data Safety Report

Below is an outline for a safety report for this trial. Tables and figures in this report are included in the appendix and are only slightly revised from those suggested by NIDDK.

I. Table of Contents
II. Narrative/ Trial Summary
    A. Summary of Main Findings
    B. Discussion of Issues or Problems
    C. Report Preparation Procedures
III. Study Description
    A. Project Organizational Chart, Personnel
    B. Brief Statement of Purpose of Trial
    C. Projected Timetable and Schedule
IV. Study Administration
    A. Recruitment Status
        1. Enrollment by Month
        2. Comparison of Targeted to Actual Enrollment
    B. Retention Status
        1. Overall Subject Status
        2. Individual Subject Status
V. Study Data Reports/Tables or Figures
    A. Generic Information
        1. Enrollment (Table 1, Figure 1)
        2. Status (Table 2)
        3. Demographics (Table 3 and 4)
    B. Safety Assessment
        1. Treatment Duration for All Subjects (Table 5)
        2. Treatment Duration for Subjects who Discontinue Treatment (Table 6)
        3. Adverse Events (Table 7)
        4. Serious Adverse Events (Table 8)
        5. Deaths (Table 9)
        6. Checklist for safety officer to complete after reviewing the safety report (Table 10)
        7. Other situations that might be of safety concern

Table 1. ENROLLMENT BY MONTH OF STUDY

Date: _____

Month	# Expected	# Screened	# Enrolled	# Withdrawn

GENERIC SAMPLE of Figure 1 shown below –
our recruitment is expected to be completed in 4 months:

FIGURE 1.
COMPARISON OF TARGET TO ACTUAL ENROLLMENT BY MONTH

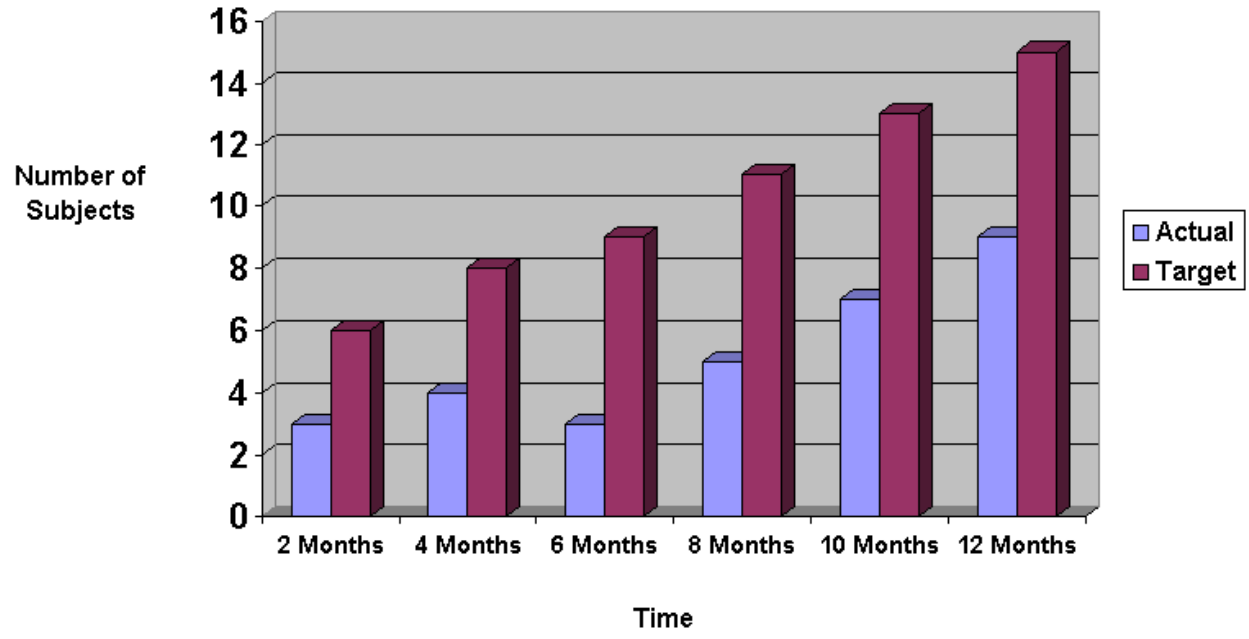


Table 2. OVERALL SUBJECT STATUS

Date: _____

	Pt. Identification	Screened	Date Enrolled	Date Completed	Active	Terminated/ Dropped Out (reason)
Total, n						

Table 3. RACE/ETHNIC CHARACTERISTICS

Date: _____

TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date by Ethnicity and Race				
Ethnic Category	**Sex/Gender**			
	Females	**Males**	**Unknown**	**Total**
Hispanic or Latino				
Not Hispanic or Latino				
Unknown				
Ethnic Category: Total of All Subjects				
Racial Categories				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Pacific Islander				
Black or African American				
White				
More than one race				
Unknown or unreported				
Racial Categories: Total All Subjects				
HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date				
Racial Categories				
American Indian/Alaska Native				
Asian				
Native Hawaiian or Pacific Islander				
Black or African American				
White				
More than one race				
Unknown or unreported				
Racial Categories: Total All Subjects				

Table 4. DEMOGRAPHIC AND KEY BASELINE CHARACTERISTICS BY GROUP

Date: _____

Characteristics	Treatment N%	Control N%	Total N%
Gender			
- Male			
- Female			
Ethnicity			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown			
Race			
- American Indian/Alaska Native			
- Asian			
- Native Hawaiian or Other Pacific Islander			
- Black or African American			
- White			
- Hispanic or Latino			
- More than one race			
- Unknown or not reported			
Age			
- Mean			
- Median			
- Minimum			
- Maximum			
Risk Factors			
Clinical Features			

Table 5. TREATMENT DURATION FOR ALL SUBJECTS

Date: _____

TIME IN STUDY	N	%	TOTAL
1 month or less			
2-5 months			
6-9 months			
10-13 months			
14-18 months			
19-23 months			
Completed study			

Table 6. TREATMENT DURATION FOR SUBJECTS WHO DISCONTINUED THERAPY

Date: _____

Time in Study	N	%	Total
1 month or less			
2-5 months			
6-9 months			
10-13 months			
14-18 months			
19- 23 months			
Completed study			

Table 7. DIVERSE EVENTS

Date: _____

Subject	Adverse Event	Onset Date	Ending Date	*Severity	*Action	*Outcome	Notes

CODES:

Severity:
1 = Mild
2 = Moderate
3 = Severe
4 = Life threatening**

Intervention Relatedness:
0 = non-Related
1 = Related

Action (taken):
0 = None
1 = Exercise modification
2 = Advice to contact PCP
3 = PCP notified
4 = Hospitalization**
5 = Other (specify under comments)

Outcome:
1 = Resolved
2 = Recovered with minor changes to daily activities
3 = Recovered with major changes to daily activities
4 = Condition still present and under treatment
5 = Condition continues to worsen
6 = Patient died**

****Event is serious and explained in detail on SAE form (DSMP Table 8)**

Table 8. SERIOUS ADVERSE EVENTS

Date: _____

Subject	Age	Treatment Date	Event	Onset Date	*Relationship	Description of Actions and Outcome (e.g., hospitalization concomitant meds, study, status, etc.)

***SAE RELATIONSHIP TO INTERVENTION**
0 = Definitely Unrelated
1 = Unlikely
2 = Possibly Related
3 = Probably Related
4 = Definitely Related

Table 9. DEATHS

Date: _____

Patient ID#	DOB	Date Enrolled	Treatment Duration	Cause of Death	Date of Death

Checklist for safety officer to complete after reviewing the safety report:

Please reply in the right column	
20% of the participants recruited non-white?	
14% of the participants recruited Latino?	
30% of participants recruited men?	
Were participants accrued at a rate of 5-6 per week in this recruitment wave?	
Do all recruited subjects meet eligibility criteria?	
Are the dropouts above 25%?	
Have potential risks been likely (occurs in >25% of people)?	
Have potential risks been infrequent (occurs in 1-10% of people)?	
Have potential risks been rare (occurs in <1% of people)?	
What is the % compliance (out of total possible) for this quarter?	
Are there any other situations that have occurred in the trial since the last safety report that warrant triggering a study investigator conference call or contact with the UNIVIESTY OF UTAH IRB or NIDDK? (If yes, please explain in the space below this checklist)	
Based on any of the replies above, is there any need to communicate with the UNIVIESTY OF UTAH IRB and/or the NIDDK regarding data monitoring or safety of participants?	
Based on your review of the safety report, is there need for discussion between study investigators regarding data monitoring and/or participant safety?	

REFERENCES

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