

Complete Title: Piloting a Reinforcement Learning Tool for Individually Tailoring Just-in-time Adaptive Interventions

Sponsor: University of North Carolina, Chapel Hill

NCT number: NCT05751993

Protocol Date: 7 April 2025

University of North Carolina, Chapel Hill

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PROTOCOL TITLE: Piloting a Reinforcement Learning Tool for Individually Tailoring Just-in-time Adaptive Interventions

Protocol Version: 1.1

Version Date: 04/07/2025

I confirm that I have read this protocol and understand it.

Principal Investigator Signature:

A handwritten signature in black ink that reads "Brooke J. Nezami". The signature is written in a cursive, flowing style.

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ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AM	Active Minutes
API	Application Program Interface
ASA-24	Automated Self-Administered 24-hour Recall
BCT	Behavior Change Technique
BMI	Body Mass Index
CES-D	Center for Epidemiological Studies Depression Scale
DSMB	Data Safety Monitoring Board
FAQs	Frequently Asked Questions
IRB	Institutional Review Board
JITAI	Just-in-Time Adaptive Intervention
JIT	Just-in-Time
MRT	Micro-randomized Trial
MVPA	Moderate to Vigorous Physical Activity
NCI	National Cancer Institute
NIH	National Institutes of Health
OCT	Office of Clinical Trials
PAR-Q	Physical Activity Readiness Questionnaire
PAQ	Paffenbarger Physical Activity Questionnaire
PRS	Protocol Registration and Results System
QEW-5	Questionnaire on Eating and Weight Loss Patterns
REDCap	Research Electronic Data Capture
RCT	Randomized Clinical Trial
SD	Standard Deviation
SSRIs	Selective Serotonin Reuptake Inhibitors
UNC	University of North Carolina at Chapel Hill
WEL-Q	Weight Efficacy Lifestyle Questionnaire

PROTOCOL SYNOPSIS

Study Title	Piloting a Reinforcement Learning Tool for Individually Tailoring Just-in-time Adaptive Interventions
Funder	National Cancer Institute
Clinical Phase	NA
Study Rationale	Epidemiological evidence suggests that excess weight is associated with at least 13 types of cancer. Weight gain from the ages of 18 to 55 is associated with increased cancer risk, and there is evidence that weight maintenance and weight loss is associated with reduced cancer risk after the age of highlighting the need to intervene in early to middle adulthood. Population-level behavioral weight management interventions that focus on obesity-related behaviors, including diet and physical activity, may lead to reduced incidence of cancer. Although exclusively mobile interventions have produced weight losses that are generally smaller than in-person treatment, mHealth technology promises opportunities for using digital health data to adaptively tailor interventions in real-time, with just-in-time adaptive interventions (JITAI) that can tailor brief interventions to meet the unique needs, behavior response patterns, and environmental contexts of the individual. Our team developed a JITAI, Nudge, that tested multiple types of just-in-time delivered messages on achievement of multiple daily weight loss behaviors: weighing, diet self-monitoring, and physical activity. The Nudge intervention was adaptive in that intervention supports relied on real-time information regarding individuals' changing behavior. However, the interventions provided in Nudge and other JITAI are based upon expert-defined fixed <i>a priori</i> decision rules that cannot be truly personalized because the same rules are applied to everyone, regardless of new information about how each participant responds to messages. Reinforcement Learning (RL), a type of machine learning, holds promise for addressing the limitations of previous approaches to implementing JITAI. Adaptive RL applications work by updating information about expected "rewards" (i.e., proximal outcomes) based on the results of sequentially randomized trials. Instead of using the fixed <i>a priori</i> decision rules to select the message, the model selects the type of message that is most likely to promote the proximal daily behaviors. This type of RL modeling has not yet been used in the context of promoting multiple weight-related daily behaviors (diet, activity, and weighing) in a comprehensive weight loss intervention. To test the feasibility of this type of modeling, we will conduct a 12-week pilot trial using a RL model (AdaptRL) that drives message choice among N=20 adults with overweight or obesity.
Study Objective(s)	• Test the feasibility of using AdaptRL in a pilot mobile weight loss study with adults. • Evaluate message delivery, including message types, over time. • Evaluate participant engagement and self-monitoring adherence during the trial. • Measure weight change (percent weight loss) over time.

Test Article(s) <i>(If Applicable)</i>	All participants will receive a core 12-week weight loss intervention that includes evidence-based lessons, behavioral skills content, and daily self-monitoring of weight, dietary intake, and physical activity.
Study Design	ADAPT is a one-group 12-week pilot study to test the feasibility of using a reinforcement learning model (AdaptRL) to inform message delivery. AdaptRL will learn over time if participants' behavioral goal achievement is more responsive to certain types of messages at certain times and under which conditions and will better inform message delivery over time. Message delivery statistics and participant engagement will be measured over time. Participants will complete assessments of weight and other behavioral and psychosocial measures at baseline and 12 weeks.
Subject Population	Inclusion Criteria 1. Age 18-55 2. Body mass index (BMI) of 25-40 kg/m² 3. English speaking and writing 4. Own a smartphone with a data and text messaging plan 5. Able to attend one study visit at the research office in Chapel Hill Exclusion Criteria 1. Type 1 diabetes or currently receiving medical treatment for Type 2 diabetes 2. Report a heart condition, chest pain during periods of activity or rest, or loss of consciousness on the Physical Activity Readiness Questionnaire (PAR-Q; items 1-4); individuals endorsing joint problems, prescription medication usage, or other medical conditions that could limit exercise will be required to obtain written physician consent to participate 3. Lost 10lbs. or more of body weight (and kept it off) in the last 6 months 4. Past diagnosis of or receiving treatment for a DSM-5-TR eating disorder (anorexia nervosa, bulimia nervosa, or other diagnosis) 5. Currently pregnant or planning to become pregnant within the next 4 months 6. Pre-existing medical condition(s) that preclude adherence to an unsupervised exercise program or the ability to walk, including history of heart attack or stroke, current treatment for cancer or treatment in the last 5 years, tuberculosis, or inability to walk for exercise 7. Health or psychological diagnoses that preclude participation in a prescribed dietary and exercise program, including history of or diagnosis of schizophrenia or bipolar disorder, hospitalization for a psychiatric diagnosis in the past year, current diagnosis of alcohol or substance abuse 8. Currently participating in a weight loss, nutrition, or physical activity study or program or other study that would interfere with this study 9. Currently using prescription medications with known effects on appetite or weight (e.g., oral steroids, weight loss medications), with the exception of individuals on a stable dose of Selective Serotonin Reuptake Inhibitors (SSRIs) for 3 months) 10. Previous surgical procedure for weight loss or planned weight loss surgery in the next year

	11. Another member of the household is a participant or staff member on this trial 12. Not willing to wear a Fitbit every day 13. Reason to suspect that the participant would not adhere to the study intervention 14. Have participated in another study conducted by the UNC Weight Research Program within the past 12 months
Number Of Subjects	20
Study Duration	Each subject's participation will last 12 weeks. The entire study is expected to last 4-6 months.
Study Phases	(1) <u>Screening</u> : screening for eligibility and obtaining consent
Screening	(2) Baseline assessment procedures
Study Treatment	(3) <u>Intervention</u> : study intervention/experimental treatment
Follow-Up	(4) Follow-up assessments at 12 weeks after start date
Efficacy Evaluations	NA (feasibility trial)
Pharmacokinetic Evaluations	NA
Safety Evaluations	All medical events and safety data will be assessed at assessment points or when interim events are reported by participants using a standard form used in our ongoing NIH funded trials.
Statistical And Analytic Plan	The primary research question of this proposal is whether it is feasible to use the AdaptRL model to derive decision rules and deliver JIT messages in the ADAPT trial. We will use descriptive statistics to examine types and frequencies of messages delivered, engagement with the ADAPT web app, and self-monitoring adherence. A secondary outcome of interest in percent weight loss among the participants from baseline to 12 weeks.
DATA AND SAFETY MONITORING PLAN	Data safety management in this trial is intended to achieve 4 objectives: 1) to minimize the occurrence of adverse effects, especially those related to intervention; 2) to effectively manage adverse events as they relate to the study; 3) to identify when the intervention should be suspended because of concerns for participant safety; and 4) to determine when interventions may be resumed after having been suspended. The Principal Investigator (PI) will have primary responsibility for the safety of participants as it relates to the study protocol, which has been approved by the UNC IRB prior to study initiation. The research team will provide continuous monitoring of participant safety and periodic reporting to the IRB as required, including any Unanticipated Problems/Severe Adverse Events that may have occurred during the study. If risk or complexity is significant, the UNC Office of Human Research Ethics may require additional reporting or alternative data and safety monitoring. Data safety and monitoring activities continue until all participants have completed treatment and until all participants have been followed to the point at which study related adverse events would likely no longer be encountered.

BACKGROUND AND RATIONALE

1.1 Name and Description of Investigational Intervention

A total of 20 adults with overweight or obesity will participate in a 12-week behavioral weight loss program delivered through the ADAPT mobile web app. ADAPT integrates data from wireless scales, Fitbit activity trackers, and the Fitbit food log, and includes evidence-based weekly lessons, tailored feedback, self-monitoring, and daily behavior change technique (BCT) messages. Participants will work toward 3 daily behavioral goals: self-weigh, an active minutes goal, and a calorie goal. Three times per day, the AdaptRL machine learning model will use participants' data to determine if they should receive a text message, and if so, what behavior (activity, dietary intake, or weighing) they should receive a message about. The objective of the trial is to test the feasibility of using the AdaptRL model to guide message delivery.

1.3 Relevant Literature and Data

Overweight and obesity are risk factors for 13 types of cancer, and population-level behavioral weight management interventions that focus on obesity-related behaviors, including diet and physical activity, may lead to reduced incidence of cancer.¹⁻⁵ While web- and mobile-based interventions are feasible, acceptable, effective and potentially scalable solutions for promoting weight loss and adoption of physical activity,⁶⁻¹¹ such interventions are plagued by declines in participant engagement and adherence over time.

Public health interventions have traditionally relied on set schedules of intervention delivery and dose that are applied to everyone. Seamless and uninterrupted collection of connected health information, such as self-monitoring data, offer unprecedented opportunities to develop more effective, dynamic and scalable health behavior interventions and hold promise for high-impact improvements in public health. Advances in computer tailoring have lessened the "one size fits all" nature of public health interventions, but they have focused primarily on the content of the intervention. New methods and intervention approaches called just-in-time adaptive interventions (JITAs) can take tailoring to a new level by varying the timing, dose, and content of the intervention to meet the unique needs, behavior response patterns, and environmental contexts of the individual.¹²

Our team developed a JITA, Nudge (NCT03836391), to promote multiple weight loss behaviors: daily weighing, dietary intake, and physical activity.¹³ We tested a pool of intervention messages to be delivered to participants' smartphones multiple times per day. Message content was based on several behavior change techniques that have proven effective in prior research (e.g., positive reinforcement).¹⁴ We established decision rules governing intervention message delivery that were based on real-time dietary, activity, and weight data. Nudge sent adaptive, personalized messages based on participants' real-time behavioral data. However, the intervention messages provided in Nudge and other JITAs are based upon expert-defined, *a priori* decision rules that remain fixed throughout the intervention, regardless of how each participant responds to the different types of messages. Reinforcement Learning (RL), a type of machine learning, holds promise for addressing this limitation by updating information about expected "rewards" (i.e., proximal outcomes) based on the results of sequentially randomized trials.^{15,16} Therefore, we have developed a reinforcement learning model (AdaptRL) that reads in and analyzes participant behavioral data, efficiently conducts micro-randomized trials and learns over time about the effectiveness of the message types, and uses decision rules that optimize daily behavioral goal achievement to determine what type of message, if any, a participant should receive at the scheduled messaging times. The objective of this study, ADAPT, is to test the feasibility of using AdaptRL in a 12-week pilot weight loss study (based on the original Nudge study) with 20 adults.

1. STUDY OBJECTIVES

Objective: Evaluate the feasibility of using AdaptRL to inform delivery of intervention messages based on a set of behavior change techniques among 20 adults in a 12-week weight loss program.

Expected outcome: A RL model, with demonstrated feasibility, capable of integrating and analyzing 3 sources of digital health data and generating unique messaging recommendations for individual participants in a behavioral weight loss program.

2. INVESTIGATIONAL PLAN

Study Design

2.1 Overview and study design

This is a one-group 12-week pilot study to test the feasibility of using a reinforcement learning model (AdaptRL) to inform message delivery. It uses participant data to learn over time, at 3 time points per day, which behavioral goal a given participant needs a message about (eating, activity, or self-weighing).

2.2 Intervention Overview

Participants will receive a 12-week weight loss program delivered through text messages and a log their calories from foods and beverages in the Fitbit app. All participants will have three daily goals: weigh daily, a daily personalized active minutes goal, and a daily calorie goal. They will receive between 0 and 3 text messages per day. At 3 pre-specified times per day (within morning, afternoon, and evening intervals), the system will use the behavioral data (overall weight change, activity, calories, and progress over time on these behaviors), and prior behavioral responses to certain types of messages, to determine if a message should be sent, and if so, what behavior-type message (i.e., whether to send a message about eating, activity, or weighing). AdaptRL will learn over time if participants' behavioral goal achievement is more responsive to certain messages at certain times and under certain conditions (e.g., weight change) and will better inform message delivery over time.

Study Population

Individuals will be eligible if they meet the following criteria: age 18-55; body mass index (BMI) of 25-40 kg/m²; English-speaking and writing; and own a smartphone with a data and texting plan. Exclusion criteria include: Type 1 diabetes or currently receiving medical treatment for Type 2 diabetes; have a heart condition, chest pain during periods of activity or rest, or loss of consciousness on the Physical Activity Readiness Questionnaire (PAR-Q; items 1-4; individuals endorsing joint problems, prescription medication usage, or other medical conditions that could limit exercise will be required to obtain written physician consent to participate); lost 10lbs. or more of body weight (and kept it off) in the last 6 months; past diagnosis of or receiving treatment for a DSM-5-TR eating disorder (anorexia nervosa, bulimia nervosa, or other diagnosis); currently pregnant or planning to become pregnant within the next 4 months; pre-existing medical condition(s) that preclude adherence to an unsupervised exercise program or the ability to walk, including history of heart attack or stroke, current treatment for cancer or treatment in the last 5 years, tuberculosis, or inability to walk for exercise; health or psychological diagnoses that preclude participation in a prescribed dietary and exercise program, including history of or diagnosis of schizophrenia or bipolar disorder, hospitalization for a psychiatric diagnosis in the past year, current diagnosis of alcohol or

substance abuse; currently participating in a weight loss, nutrition, or physical activity study or program or other study that would interfere with this study; currently using prescription medications with known effects on appetite or weight (e.g., oral steroids, weight loss medications); previous weight loss surgery or planned weight loss surgery in the next year; another member of the household is a participant or staff member on this trial; not willing to wear a Fitbit every day; reason to suspect that the participant would not adhere to the study intervention; have participated in another study conducted by the UNC Weight Research Program within the past 12 months.

3. STUDY PROCEDURES

Data Collection

Assessments will be completed at baseline and follow-up and assessed online unless otherwise noted, and message delivery and participant engagement will be measured throughout the 12-week study period. Participants will receive a \$30 gift card for completing the 12-week assessment.

Measures

Primary Outcome Measures (collected daily)

- **Feasibility of AdaptRL.** Feasibility is defined as the mean number of messages delivered per participant per day. Message analytics, including type of message, time delivered, and all data required to run the RL policy are tracked daily by the ADAPT system.
- **Study engagement.** Study engagement will be defined as percent of program days accessing the ADAPT web app page views will be tracked at the observation level and summed to report each participant's total days accessing the web app.
- **Self-monitoring adherence.** Self-monitoring adherence at the daily level is defined as engaging in at least one self-monitoring behavior on a given day (tracked calories, wore tracker, or self-weighed). Data will be used to calculate the percent of program days with self-monitoring adherence.

Secondary Outcome Measures

- **Percent weight loss.** Participants will complete official weight measurements using the study-provided Fitbit scale at their home. Participants will be asked to weigh themselves three times in a row, upon waking and before eating, in light clothing, without shoes, and the three weights will be averaged and used to calculate percent weight change over time. Percent weight loss will be defined as weight change from baseline to 12 weeks calculated as a percent from baseline weight.
- **Moderate-to-vigorous physical activity (MVPA).** MVPA at baseline and 12 weeks will be assessed with the self-reported Paffenbarger Physical Activity Questionnaire (PAQ) which assesses leisure-time activity and provides an estimate of minutes per week of moderate-to-vigorous intensity, and calories/week of light (5 kcal/min), medium (7.5 kcal/min), and high (10 kcal/min) intensity activities (Paffenbarger et al., 1978).
- **Dietary Intake.** Self-reported daily caloric intake will be assessed using the NCI's Automated Self-Administered 24-hour Recall (ASA-24; National Cancer Institute) at baseline and 12 weeks. Participants will complete two unannounced self-reported recalls; one weekday and one weekend day. Daily caloric intake is measured in kcals, with higher numbers indicating higher caloric intake.
- **Adherence to calorie goal.** Participants will have a daily calorie goal that is determined by their sex and baseline weight. Daily caloric intake will be calculated from participants' recorded calories in the Fitbit app. We will calculate a dichotomous outcome of whether a participant stayed at or under their calorie

goal (NOTE: days with < 800 calories tracked are counted as not meeting the calorie goal). This data will be used to calculate each participant's percent of days meeting the calorie goal.

- **Adherence to daily active minutes (AM) goal.** Participants will have a daily AM goal that may change or stay the same at the beginning of each program week. Fitbit trackers will be used to collect daily AM data, defined by Fitbit as physical activity of at least moderate-to-vigorous intensity that is accumulated in 10-minute bouts. We will calculate a dichotomous outcome of whether a participant met their daily AM goal (days with no tracker wear are counted as not meeting the goal) each day of the program. This data will be used to calculate each participant's percent of days meeting the daily AM goal.
- **Adherence to daily weighing.** Fitbit scale data will be used to create a dichotomous outcome of whether a participant weighed or not each day of the program. This data will be used to calculate each participant's percent of days weighing.

Other Measures

- **Binge Eating.** Participants will complete the revised Questionnaire on Eating and Weight Patterns (QEWP-5) to assess the frequency of binge eating, loss of control, and compensatory behaviors.¹⁷
- **Depression.** The Center for Epidemiologic Studies Depression Scale (CES-D) is a self-report depression scale designed to measure depressive symptoms in the general population.¹⁸ This 20-item self-test measures depressive feelings and behaviors during the past week. It will be administered during the in-person assessment visits at baseline and 30 days. Questionnaires will be scored on-site. Individuals scoring greater than 16, indicating levels of depressive symptoms that might benefit from follow-up with a health care provider, will be given a letter explaining the survey and providing information and referral.
- **Self-efficacy for physical activity.** This will be measured using the Self-Efficacy for Exercise Questionnaire developed by Sallis and colleagues.¹⁹ This 12-item measure assesses self-efficacy for exercise related to resisting relapse and making time for physical activity.
- **Self-efficacy about eating behavior in the context of weight loss.** This will be assessed using the Weight Efficacy Lifestyle Questionnaire (WEL-Q; Clark et al., 1991).²⁰ The 20-item scale consists of 5 situational factors, with internal consistencies ranging from .70 to .90. Clinical treatment studies have shown the WEL to be sensitive to changes in global scores and individual factor scores.
- **Competence for diet and physical activity.** The Perceived Competence for Diet and Physical Activity Scale includes 4 items that measure perceived competence for diet and 4 items for physical activity. Items are rated on a 7-point scale from 1 (not at all true) to 7 (very true), for example. "I feel confident in my ability to maintain a healthy diet."
- **Sociodemographics and health-related variables.** Basic demographic information, including age, sex, race, education level, and income, will be assessed at baseline only using a standard demographic questionnaire. The questionnaire will also assess smoking history, medication use, alcohol use, and prior use of smartphones and physical activity trackers.
- **Weight history.** At baseline only, participants will complete a questionnaire reporting their weight history, including information about their weight goals and whether they have dieted in the past or participated in other weight loss programs.
- **Medical events.** At follow-up only, participants will be asked about exercise-related or other injuries or hospitalizations during the study period.

4. STATISTICAL CONSIDERATIONS

Sample Size and Power

There is no formal power analysis given that this is a one-group intervention that is testing the feasibility of a newly developed reinforcement learning model. However, We will have 80% power to detect a 6% decrease in body weight with a Type I error rate of .05.

Statistical Analysis Plan

Baseline demographic and descriptive characteristics will be summarized globally, using frequencies and percentages for categorical variables, and means and standard deviations (SD) for continuous variables. Prior to conducting data analyses, we will audit the data for completeness and quality, including missing data. We will evaluate response distributions to ensure that they meet assumptions of planned analyses (see below), including the detection of outliers.

Analysis of primary outcomes

We will use descriptive statistics to evaluate: 1) the mean number of messages delivered per participant per day as a result of the AdaptRL model (feasibility), 2) the mean percent of person-days in which participants accessed the web app (study engagement), and 3) the mean percent of person-days in which participants tracked at least one weight loss behavior (tracked calories, wore tracker, or self-weighed; self-monitoring adherence).

Analysis of secondary outcomes

We will also calculate: mean percent weight change from baseline to 12 weeks, change in self-reported MVPA from baseline to 12 weeks, change in daily caloric intake from baseline to 12 weeks, adherence to the calorie goal, adherence to the daily active minutes goal, and adherence to daily self-weighing.

5. SAFETY MANAGEMENT

Data safety management in this trial is intended to: 1) minimize the occurrence of adverse effects, especially those related to intervention; 2) effectively manage adverse events; 3) identify when the intervention should be suspended because of concerns for participant safety; and 4) determine when interventions may be resumed after having been suspended. The Principal Investigator (Nezami) will have primary responsibility for the safety of participants as it relates to the study protocol, which has been approved by the UNC IRB prior to study initiation. Because the risks to subjects participating in this study are expected to be low, there is no formal Data Safety Monitoring Board. The research team will provide continuous monitoring of participant safety and periodic reporting to the IRB as required, including any Unanticipated Problems/Severe Adverse Events that may have occurred during the study. If risk or complexity is significant, the UNC Office of Human Research Ethics may require additional reporting or alternative data and safety monitoring. Data safety and monitoring activities continue until all participants have completed treatment and until all participants have been followed to the point at which study related adverse events would likely no longer be encountered.

Participant Safety

The risks to human subjects in this study, including psychological and physical risks, are judged to be minimal. The anticipated benefits are great, insofar as the results will be used to determine if a RL model

can result in variable, more effective messaging within a mobile-delivered behavioral weight loss intervention. The primary risks, while minor, include: discomfort with being asked about personal information related to their diet, physical activity, and weight; risks of increasing physical activity (injuries, blood pressure changes, dizziness, fainting, fatigue, and in very rare cases heart attack, stroke, or even death); a low risk of extreme dieting and/or extreme psychological reaction to dietary restriction; risk of breach of confidentiality via telephone calls, emails, text messages, or the smartphone app.

Adequacy of Protection Against Risks

a. Informed Consent and Assent

Recruitment and Informed Consent: The UNC IRB has approved the study protocol and has reviewed and approved the informed consent document. Once an individual has been deemed potentially eligible to participate through online and telephone screening, study staff will provide more study details and assessment procedures over the telephone. Individuals who remain interested will receive an email directing them to a unique and secure REDCap link to an online informed consent. After clicking on the link, they will be directed through a series of screens that present the informed consent document. The online informed consent records will be retained, and recruitment of participants will be done by adhering to HIPAA regulations. Accrual reports will list enrolled participants and excluded participants throughout the stages of the research. This routine monitoring allows for early identification and resolution of potential problems during the recruitment phase. The anticipated recruitment duration is 1 month. All key personnel have attended the required courses on human subject protection and HIPAA regulations, and certificates of IRB training completion are on file with the University of North Carolina.

b. Protections Against Risk

Protections against Psychological Risks: Participants will be encouraged to contact the Principal Investigator if they feel they have incurred any emotional distress as a result of study participation. As this is a voluntary study, a participant is free to exit at any point if discomfort should occur. Individuals scoring >16 on the Center for Epidemiological Studies Depression Scale (CES-D) at baseline or 12-week assessments (indicating levels of depressive symptoms that might benefit from follow up with a health care provider) will be given a letter explaining the survey and providing information and referral to resources.

Protections against Physical Risks: During the screening process, potential participants will be evaluated to determine whether it is safe for them to participate in the planned intervention. Medical problems that increase risk of study participation are assessed through questionnaires and telephone interviews prior to study start. The goal of these assessments is to detect conditions by history, such as recent heart attack; symptomatic conditions such as weight-bearing pain; and asymptomatic conditions such as eating disorders.

To ensure medical readiness to begin physical activity, participants will complete a Physical Activity Readiness Questionnaire (PAR-Q). The PAR-Q assesses the following medical conditions: heart problems, chest pains, faintness or dizzy spells, high blood pressure, bone or joint problems such as arthritis that has been or could be aggravated by exercise, prescription medication use, and other medical reasons why exercise would not be advisable. Participants endorsing any items on the PAR-Q will be excluded from the study, as these pre-existing medical conditions preclude adherence to an unsupervised exercise program.

Participants who develop musculoskeletal problems or other health problems that may affect the safety of the intervention will be instructed to stop exercising until the problem resolves and their physician approves resumption of physical activity. The consent form will indicate that UNC has not set aside funds to pay for any personal injuries should any occur, or for related medical care, and that any costs for medical care will be the responsibility of the participant.

All participants will be advised about safe weight loss practices, including dietary change and increasing physical activity, at their initial study visit. Participants will be advised to gradually increase their physical

activity and to use walking as a primary form of activity, and will be taught that the appropriate rate of weight loss is 1 to 2 pounds per week.

In addition, we will carefully monitor changes in weight during our trial. We will collect information at each assessment time point on hospitalizations for any psychiatric problem, including depression and eating disorders. We will track weight changes using smart scale weights and will identify any individual who loses more than 20% of their body weight, has a BMI of 18.5 kg/m^2 at any point during the program, or loses more than 15 pounds in any month during the trial. We will have a telephone call with these participants within 2 weeks, discuss our concerns with them, and make referrals if appropriate. If there is no improvement in weight status, the participant will be unable to continue to participate in the intervention.

Protections to Ensure Confidentiality of Participants: All data records related to a participant's involvement in this research study will be stored in encrypted files on servers that adhere to the University policy on storage and transmission of sensitive data. Participant identity on these records is indicated by an ID number and the information linking these numbers with participant identity will be kept separate from the research records. In addition, all research databases will have password-controlled access.

The Fitbit API will be used to access data from participants' scale, activity tracker, and Fitbit app. During the consent process, participants will consent for data from their specific device IDs to be accessed by our study. They will need to enter their Fitbit username and password during the app setup process to allow Fitbit data to be sent to our study server. The study smartphone app uses a standard OAuth 2.0 security model for logging in to Fitbit. The study uses temporary access tokens that are stored only on the user's device and are not stored on our servers. Therefore, Fitbit usernames and passwords will not be stored in any way with this study. Instead, the weight and tracker data will be connected to participants by their unique study ID, which they will also enter during the app setup process. Data are transmitted on secure servers that adhere to University policy on Sensitive Data.

The risk of breach of confidentiality over the Fitbit websites will be partly subject to each individual's comfort in sharing information in their individual profile. To further minimize the risk of breach of confidentiality, all participant activities on the Fitbit websites will be voluntary. Consent forms will also clearly communicate the risk of this type of disclosure to participants.

Removal of Patients from Protocol. Participants will be removed from the protocol should they experience greater than minimal risk as detailed above. Participants will be reminded that their participation is voluntary and that they may withdraw from the study at any time without consequence by contacting the Principal Investigator. In addition, we will stop all intervention activities for anyone who becomes pregnant.

6. DATA COLLECTION AND MANAGEMENT

Participants will provide physical data (objective weight and self-reported height) and self-reported questionnaire data online specifically for research purposes using the REDCap computer-assisted program that has built-in validation checks for range, data type, and completeness. All measurements will undergo consistency and outlier checks, compared with raw data, and edited as required. REDCap includes detailed audit logs that document any database changes, and we will document protocols for cleaning data. Identifiable information collected in online surveys will include the participant's name, address, phone numbers, and date of birth. Food log, weight, and activity data from Fitbit will be transmitted to study servers.

7. RECRUITMENT, CONSENT, AND RETENTION STRATEGY

Recruitment

Participants will be recruited using 1) the UNC email listserv and 2) Facebook and Instagram (Meta) advertising (sponsored posts). Participants will self-select if they are interested. We will purchase Meta advertisements and “Sponsored Posts” with recruitment information about the study that will link to the recruitment website and online screening survey. The ads and sponsored posts will be targeted specifically to reach adults between the ages of 18 and 55 that live in the Raleigh/Durham/Chapel Hill area and can also be targeted specifically to reach only men and minorities, if needed. We have successfully recruited adults in the Chapel Hill area for prior studies, so we believe we can easily recruit 20 participants for this small pilot study.

All individuals who respond to our advertising will be eligible for enrollment independent of sex or gender and race/ethnicity. As women are generally over-represented in weight control studies, we do not anticipate having inadequate representation by women. The large geographic radius that will be used to target the Facebook ads is intended to reach a more diverse population living outside of the immediate Raleigh/Durham/Chapel Hill metropolitan area, which may lead to a higher representation by minorities. In past studies, we have successfully recruited minority populations. For the current trial we will aim to recruit at least 50% non-white participants, with specific emphasis on Black and Hispanic populations, given the burden of overweight in these groups. Initially, no groups will be excluded or limited based on sex/gender, race, and or/ethnicity. However, if the enrollment targets for minority participants are proceeding slower than expected compared to white participants, we may limit enrollment of white participants in order to raise the percentage of minority participants closer to our targets.

All recruitment efforts will direct participants to a study website with a more detailed description of the research study and FAQs about participating in research. Interested individuals will click through to a REDCap web screening survey to determine initial eligibility. Those who are preliminarily eligible will be contacted by trained study staff and will undergo additional phone screening. Eligible and interested individuals will receive an email directing them to a unique REDCap link to an online informed consent. After providing consent, participants will be instructed on procedures for 1) completing one weekday and one weekend self-reported 24-hour dietary recall, 2) completing baseline online questionnaires, 3) picking up their Fitbit scale and tracker from the research clinic, and 4) completing their baseline weight measurement using the Fitbit scale. After completion of baseline assessments, the participant will be scheduled for a group video kickoff session during which they will be informed about study procedures, assisted with logging into the study smartphone app, and questions about getting started will be answered.

Retention

A systematic protocol will be followed to minimize dropouts. At baseline, the names and addresses of several friends and family members who can be contacted are obtained for use if we lose touch with the participant and need to contact them for study assessment completion. The study provides a \$30 incentive for completing the follow-up assessment to offset any time costs and to promote retention. For the final (12-week) assessment visit, we will send participants an email that will include a link to online questionnaires with an expected completion date as well as a scheduled date and time to step on their scale for their final weight assessment. Missed weights and/or calls will be immediately followed up by phone and rescheduled.

8. PLANS FOR PUBLICATION

As Principal Investigator of this grant application and clinical trial, Dr. Nezami will comply with the clinical trial information dissemination expectations of the NIH policy to register and submit summary results at ClinicalTrials.gov. Consistent with the terms and conditions of NIH funding, we will ensure the submission and updating of registration and results information for this clinical trial in the timeframes established by

the Final Rule. Registration and results reporting in ClinicalTrials.gov will be completed within the following timeframes:

- Registration of the trial at ClinicalTrials.gov no later than 21 days after enrolling the first participant.
- All submitted information will be updated at least once a year.
- Any apparent errors, deficiencies, and/or inconsistencies identified by NIH as part of the quality control review process and any other errors identified will be addressed by the responsible party.
- Corrections to submitted information will be made within 15 days for registration information and 25 days for results information.
- Trial results will be submitted no later than one year after the primary completion date.

Informed Consent Documents for the clinical trial will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov. The UNC IRB has template language explaining that the study will be posted on ClinicalTrials.gov that investigators are required to include in the consent document for the trial.

As PI, Dr. Nezami will work closely with the UNC-CH Office of Clinical Trials (OCT), which serves as the university's internal PRS. The OCT has responsibility for ensuring that clinical trial registration and reporting occurs in compliance with NIH policies. The OCT has support staff to facilitate the process of registration and results reporting to ClinicalTrials.gov, and our team will work closely with them to register this trial and to submit summary results to the website in a timely manner, in keeping within the required timeframes. Once data collection is complete, our research team will work to prepare and submit trial results no later than one year after the primary completion date.

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