A Multiple Health Behavior Change Intervention for Overweight and Obese Smokers

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Study Protocol

Title: A Multiple Health Behavior Change Intervention for Overweight and Obese Smokers

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Brief Summary and Description

The purpose of this study is to conduct a pilot study as part of a Career Development Award (K23) funded through NIH. We will recruit overweight or obese (OB) cigarette smokers (BMI ≥ 25) to participate in 8 weeks of either a self-regulation weight gain prevention intervention (SR; an intervention based on self-regulation approaches to produce and maintain weight loss shown to be effective for weight gain prevention) or lifestyle education (LE; attention-placebo control) followed by 8 weeks of smoking cessation treatment. We will conduct a small RCT with 60 OB smokers comparing SR to LE, with both conditions subsequently receiving smoking cessation counseling and combination nicotine replacement therapy to assess intervention feasibility and acceptability and obtain preliminary effect size data. Up to 60 OB smokers from the community will participate in 8 weeks of group weight gain prevention (self-regulation plus large changes in behavior) or lifestyle education (attention-placebo control) followed by 8 weeks of group smoking cessation treatment with nicotine replacement therapy as part of an RCT. Assessments will occur at baseline, week 9 (quit day), 1 month post-quit, 2 months post quit, and 3 months post-quit.

Specific Aims

We aim to conduct a small RCT with 60 OB smokers comparing SR to LE, with both conditions subsequently receiving smoking cessation counseling and combination nicotine replacement therapy to assess intervention feasibility and acceptability and obtain preliminary effect size data regarding the following hypotheses: Smokers in the SR vs. LE condition will have better biochemically verified point-prevalence abstinence from smoking at the end of smoking cessation treatment and at follow-ups, with a medium effect size. Smokers in the SR vs. LE condition will have less weight gain at the end of smoking cessation treatment and at follow-ups, with a medium effect size.

We will also examine potential mechanisms of action for efficacy of SR on improved smoking outcomes, expecting that: Smokers in the SR vs. LE condition will have greater increases in self-efficacy for managing weight and for quitting smoking and greater decreases in negative affect and delay discounting prior to quitting. Self-efficacy, negative affect, and delay discounting will be associated with abstinence at follow-ups.

Methodology

Project Purpose

This project focuses on collecting pilot data to inform a larger clinical trial for preventing weight gain and improving smoking cessation outcomes in overweight and obese smokers who are disproportionately at risk for disease, disability, and premature death but may be reluctant to give up smoking due to the fear of subsequent weight gain and trouble managing their weight without cigarettes. Helping these individuals lose weight prior to quitting smoking could provide a buffer against post-cessation weight gain and may improve mood, help increase the salience of future health outcomes, and increase self-efficacy for tackling the challenges associated with quitting smoking. Use of a multiple health behavior change intervention can maximize anticipated health benefits of smoking cessation and reduce the potential for relapse to smoking due to post-cessation weight gain. With an effective program, more overweight or obese smokers may be willing to attempt smoking cessation which could impact the two leading causes of preventable mortality in the US.

Project Description
Overweight and obese smokers who want to quit smoking and minimize weight gain will be assigned to one of two experimental conditions before entering smoking cessation counseling in a between-groups design in order to determine study feasibility and provide preliminary data on change in weight and abstinence from smoking. Participants will be assigned to either weight gain prevention (self-regulation plus large changes in behavior) or lifestyle education (attention-placebo control) for 8 weeks. Afterward, both groups will participate in 8 weeks of smoking cessation with combination NRT (transdermal patch and lozenges). Participants will begin using lozenges at week 6 (pre-quit). Both groups will participate in 8 weeks of smoking cessation with combination NRT (transdermal patch and lozenges) starting at week 9. Treatment will begin once the identified number of participants to form a group has been recruited. Assessments will occur at baseline, at week 9, and 1, 2, and 3 months after the target quit date.

Participant Population
Inclusion/exclusion criteria. The participants will be adult men and women 18-75 years old.
Inclusionary criteria are:
a) BMI 25 kg/m2
b) smoked ≥ 5 cigarettes/day during the past year
c) self-reported motivation to quit smoking
d) self-reported desire to prevent or minimize weight gain during smoking cessation
e) ability to understand informed consent
f) access to a smart phone or tablet
Exclusionary criteria are:
a) current smoking cessation or weight loss treatment/medication
b) more than 1 day/week use of tobacco or nicotine from sources other than cigarettes (other than non-daily use of e-cigarettes in addition to combustible cigarettes)
c) weight loss of 20 lbs or more within the past 6 months
d) self-reported diagnosis or treatment for an alcohol or substance use disorder within the past 6 months (with the exception of maintenance therapies)
e) endorsing recent symptomology suggestive of an eating disorder, an alcohol or substance use disorder, severe depression, or suicidal ideation
f) self-reported diagnosis or treatment or evidence of an eating disorder or severe psychiatric disorder (e.g., schizophrenia or bipolar disorder)
g) not stabilized on psychotropic medications
h) current use of medications known to interact with smoking cessation
i) clinically significant medical condition.
Physicians of individuals with type 2 diabetes or controlled hypertension will approve study participation of interested individuals and will attest that they will be responsible for any medication adjustments that are needed.

Procedures
OB smokers (n=60) will be randomized to either a combined self-regulation plus large changes (SR) intervention in advance of smoking cessation treatment condition (n=30) or to a healthy lifestyle education (LE) in advance of smoking cessation treatment attention-placebo control condition (n=30) for 16 weeks. The study will include up to 18 groups each run in succession with approximately 4-6 participants recruited for each group in order to have 3-5 participants beginning each group. Groups will be randomly assigned to one of the two treatment conditions using a random number generator after participants have completed all pretreatment assessments. Participants will learn their condition assignment at the first treatment session. Feasibility and acceptability will be monitored. Assessment of smoking/abstinence and weight will be obtained at baseline, on Quit Day, and 1, 2, & 3-months post-quit.

Recruitment procedures- Participants will be recruited through print and electronic advertising (e.g., newspaper, magazine, listserv, websites, online ads), advertisements on buses or at bus stops, and via community outreach (e.g., providing study information and pamphlets to local physicians).

Initial screening: Interested individuals will be given several options for contacting the study and for completing initial eligibility screening depending on advertising modality (e.g., call the study telephone number, email the study email address, provide their contact information in an electronic interest form). Individuals will be given the option of either completing initial screening using an online screener or being contacted by study staff for telephone screening.

> Phone screening: Individuals who are screened over the telephone will be contacted by study staff. They will be provided with a brief description of the study, and will be asked if they are interested in participating. Verbal consent will be obtained prior to the potential participant's completion of the phone screen using a bulleted consent form that includes key information. Individuals who indicate that they would like a copy of the consent document will be provided a copy via email.
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> Online screening: Online screening will be conducted using Brown's Qualtrics survey software. Individuals who are screened using an online screener will be provided with the same brief description of the study used in the phone screening. They will then review verbal consent information (bulleted points reviewed via telephone) and agree to be screened. Individuals who indicate that they would like a copy of the consent document will be able to download a copy. Those who agree to participate will be redirected to a screening questionnaire. Individuals who complete the online screener will be contacted via phone or email to provide any necessary clarifications to their screening questions and proceed to the next step of enrollment if eligible.

Online orientation session: Those who are deemed eligible on initial screening and interested will be scheduled for a brief study orientation and information session. This session will occur using the video conferencing platform Zoom. During the orientation session, the study will be described. Participants will be asked to generate pros of cons of participating using the Methods-Motivational Interviewing (MMI) approach. The MMI method has been used to improve study retention by helping participants consider pros and cons of participating prior to enrolling in a research study.

Screening, consent and enrollment, and baseline assessment: Individuals who complete the orientation session and remain interested in participating will be offered the opportunity to be scheduled for a full baseline assessment remotely using Zoom. Electronic informed consent will be obtained after the potential risks and benefits of participation are explained. Participants will be asked to provide the names of at least two family members or friends who could help us locate them at follow-up if we are unable to reach them. After informed consent, full screening will occur followed by baseline assessments for those who are eligible.

Interventions- The treatment will consist of 16 weekly, 60-minute, group sessions that will take place remotely using Zoom. The treatment will consist of 16, manualized, weekly sessions. The first 8 sessions will focus primarily on SR or LE (sessions 1-8) according to assigned condition with Quit Day preparations incorporated into weeks 7 & 8. The second 8 sessions (sessions 9-16) will focus primarily on smoking cessation and will also include brief discussions of weight and review of previously covered SR and LE topics according to assigned condition. Participants will be sent session handouts, a scale, and other intervention materials such as nicotine replacement therapy. In rare or extenuating circumstances, if a participant needs study materials in a time-sensitive way, they may be offered the opportunity to purchase these materials and be reimbursed via a ClinCard. The treatment groups will be led by study interventionists. All interventionists will be trained to provide treatment in both arms of the study. Study

interventionists will be postdoctoral fellows, clinical/counseling graduate students, or hired staff with backgrounds in clinical/counseling psychology, social work, nutrition, or another related field with intervention experience. Interventionists will be under the supervision of PI, a licensed clinical psychologist, with guidance from mentors as needed. Based on interventionist availability, if needed, the PI may also serve as an interventionist.

Self-regulation plus large changes in behavior (SR). The active intervention is based on self-regulation theory and is similar to interventions tested previously and shown to be effective in reducing weight gain and weight regain. The initial 8-week program will include weekly group sessions focused on teaching self-regulation and efforts to produce a 10 lb weight loss to buffer against anticipated post-cessation weight gain based on the SR approach. The key concepts of the intervention: Self-Regulation. Participants will be taught the core self-regulation skills for controlling their weight: a) weighing themselves daily; b) detecting small changes in weight as soon as they occur; c) implementing problem-solving skills and learned strategies to combat changes in weight; d) evaluating the success of strategies implemented; e) rewarding themselves for successful weight loss and weight maintenance or f) making behavioral changes if weight gain occurs. These strategies are introduced over the course of the 8 weeks, with the initial weeks stressing the importance of daily self-weighing and learning to use the scale for information (rather than self-evaluation). At the end of the initial 8 weeks, the participants will be introduced to a color-coded system to help them accomplish steps b-f of the self-regulation model. The goal for the first 8 weeks of the program will be to lose 10 lbs in order to buffer against expected weight gain. To accomplish this, participants will be given a reduced calorie goal (1200-1500 kcal/day if <200 lbs or 1500-1800 kcal/day if >200 lbs). They will be instructed to self-monitor their intake and taught strategies for reducing caloric intake (e.g. reducing fat content of foods) and strategies for dealing with high-risk situations such as eating out. Structured physical activity, which is activity similar in intensity to brisk walking that lasts at least 10 minutes, will also be prescribed and self-monitored, starting with a goal of 50 minutes per week (10 minutes per day on 5 days per week) and gradually increasing to 150 minutes per week.

Weeks 9-16 will focus on smoking cessation, but each session will include a private weigh-in and brief group discussion of strategies to maintain weight loss and prevent post-cessation weight gain. To maintain the weight losses achieved thus far and prevent post-cessation weight gain, participants will be taught to use a color zone system (Red, Yellow, Green) for weight maintenance to guide their behavior after completing the initial 8-week weight control program. The weight goals used to define the zones will be individually tailored based on the initial weight changes. Participants will be encouraged to weigh themselves daily and at the end of each week and to assess their current weight relative to their individual color zones. If participants are in Green, they will be encouraged to reinforce their success (with a sticker or small amount of money); if they are in Yellow they will be taught to begin monitoring their behavior more carefully and identify area to make changes to get back on track; if they are in Red, they will be encouraged to return to full self-monitoring of intake and activity and resume their original calorie intake and goals. During smoking cessation, the goal will be to minimize weight gain for those who achieved targeted weight loss as well as for those who did not. This Red, Yellow, Green system for weight maintenance has had demonstrable success in prior studies of the self-regulation model.

Healthy lifestyle education attention-placebo control (LE). Participants in this group will be provided with information on the obesity epidemic and the importance of a healthy lifestyle to use at their own pace as they wish. They will receive basic education about principles of healthy eating (e.g., simple vs. complex carbohydrates) and physical activity during the first 8 sessions. During sessions 9-16, the focus will be on smoking cessation. Sessions will also include lifestyle education information such as why weight gain occurs after smoking cessation. This group will not be taught any specific behavioral self-regulation skills to help them change their behaviors. Providing basic education about diet and exercise has produced minimal weight loss in other clinical trials.

Counseling for smoking cessation. A combination of behavioral treatment and medication is recommended according to clinical practice guidelines. Treatment elements associated with greater odds of success such as support and problem-solving skills will be incorporated throughout the counseling. Participants will be introduced to smoking cessation counseling beginning at week 7. While weeks 7 & 8 remain predominantly focused on creating a weight loss buffer (SR) or learning healthy lifestyle information (LE), approximately 20 minutes of each of these sessions will be dedicated to preparing participants to quit smoking. This will include providing basic information about smoking and successful quitting (e.g., the addictive nature of smoking, the fact that smoking even a puff increases the likelihood of relapse, typical symptoms and duration of withdrawal, benefits of quitting, importance of removing cigarettes from the environment) and encouraging participants in their quit attempts. Participants will be asked to determine a plan for high-risk situations and will be taught behavioral self-management strategies (i.e., avoid, alter, alternative), and cognitive coping strategies such as using self-statements (e.g., benefits of quitting, statements of determination). Participants will be instructed to start using NRT lozenges beginning at week 6 (pre-quit). The will begin using combination NRT (patch + lozenge) on the morning of their Quit Day which coincides with their 9th treatment session (NRT procedures below). Post-quit sessions (weeks 9-16) will focus on reinforcing success, providing encouragement, coping with cravings, discussing reactions to quitting and to NRT, problem solving, dealing with slips, planning for high-risk situations, encouraging the use of social support, and noting benefits of quitting. A brief portion of each smoking cessation session will include continued discussion of self-regulatory weight gain prevention or healthy lifestyle education information. If conducted remotely, participants may be mailed a device to monitor their CO.

The smoking intervention will also include a texting component to provide additional support to participants as they prepare to quit smoking and during smoking cessation (study weeks 8-16). This intervention will be administered by LiveInspired, a company with extensive experience in providing text messaging services, using TextMyQuit (TMQ). Participants will receive on-demand support and encouragement by texting “crave” or “slip”.

NRT procedures. NRT will be mailed to participants. Participants will be counseled on the proper use of NRT before initiating use with ample opportunity to ask questions and written materials (e.g., how to use it, precautions for use, possible side effects, storage information, what to do if a dose is missed or certain unwanted symptoms occur).

Participants will receive 3 weeks of pre-quit, preparation-phase, nicotine mini-lozenges dosed per mini-lozenge labeling (smoke within 30 min of waking, 4 mg; smoke more than 30 min after waking, 2 mg). Participants will be instructed to use one mini-lozenge every 1–2 h and up to 12 daily, with a goal of using at least 5 daily. Participants will be advised to try to reduce their smoking, reduce the range of contexts in which they smoked, and substitute mini-lozenges for cigarettes during the preparation phase consistent with past research (e.g., Piper et al., 2018).

Beginning on their target Quit Day, participants will be encouraged to use an average of 9 mini-lozenges/day, unless they experienced negative side effects (as described in informed consent and during treatment). Participants will be encouraged to taper their mini-lozenge use to zero over weeks 6-8.

Participants will receive 8 weeks of nicotine patch starting on their target quit day (participants who smoke >10 cigarettes/day: 4 weeks of 21 mg, 2 weeks of 14 mg, and 2 weeks of 7 mg nicotine patches; participants who smoke ≤10 cigarettes/day: 6 weeks of 14 mg, and 2 weeks of 7 mg nicotine patches). Use and side effects of NRT will be queried weekly post-quit.

Ensuring integrity of counseling. Sessions will be audio recorded to ensure fidelity to manualized session content as discussed with participants during informed consent procedures. PI will hold supervision

meetings with the interventionists following review of audio from the sessions. Feedback will be given to interventionists to keep delivery consistent and prevent drift, and ensure that treatment is delivered competently (e.g., appropriate flexibility, understanding of the participant, empathy).

Assessment. All assessments will be conducted by research assistants blind to intervention condition. Participants will be compensated $30 for the baseline screening session, $35 for their assessment on Quit Day, and $40, $45, and $50 for the 1, 2, and 3-months post-quit assessments, respectively. Participants will receive a completion bonus of $10 for completing each post-Quit Day assessment within 2 weeks of the specified date (up to $30). Schedule of assessment by time point is included in Table 1. Participants can choose to be paid via a ClinCard (mailed to the participant) or using an Amazon electronic gift card (sent electronically via email).

Initial screening: Age, height, weight, number of cigarettes per day, days of other tobacco products in last month, current use of any smoking cessation method, current use of other nicotine or tobacco products, access to a smart device, current addiction treatment, screening for selected medical and psychiatric problems, changes in psychiatric medications, recent or planned pregnancy or nursing, recent dieting and weight loss or weight gain, and degree of desire to quit smoking and to minimize weight gain, both assessed using Likert scales (0 = not at all, 10 = extremely).

Screening at baseline: 1. Height and weight to calculate BMI. 2. Screening interview- Age, number of cigarettes per day for past year, use other nicotine or tobacco products, current smoking cessation or weight loss treatment/medication. 3. Medical conditions and medications screening tool will be used to screen for recent medical, substance-related, or psychiatric hospitalizations and any medical conditions or medications that warrant exclusion for safety (determined by PI and study Medical Monitor). 4. Participants will complete questionnaires to assess for symptoms of disordered eating (Eating Disorders Assessment (EDA), severe depression or suicidality (total score ≥ 20 or question 9 score ≥ 1 on the Patient Health Questionnaire 9-item depression index (PHQ-9), reviewed by clinician), or substance or alcohol use disorders (CAGE-AID score ≥ 2, reflecting past 6 months). 5. Salivary cotinine and/or exhaled carbon monoxide (CO) to confirm smoking status.

Feasibility. In order to quantify feasibility of recruitment and enrollment during pilot testing the number of participants screened and enrolled will be documented per month during periods of active recruitment. The proportion of enrolled participants completing planned assessment sessions will be calculated.

Acceptability. Treatment attendance- Attendance at all counseling sessions will be recorded. Percentage of participants completing each treatment session will be calculated to examine treatment-specific retention rates. Participant Feedback- Participants will complete brief assessments at weeks 9 & the end of treatment (month 2) to assess: 1) helpfulness of interventionist, 2) perceived clinical usefulness, 3) personal relevance, 4) level of engagement, and 5) overall satisfaction scored 1 (not at all) to 5 (extremely) on a Likert-scale. Data on acceptability of other aspects of intervention (e.g., group component, pre-quit NRT, nicotine patches, nicotine lozenges, and smoking text messages) will also be assessed using a 5-point Likert scale. Participants will also be asked to provide brief feedback on sessions after each session.

Patient adherence. Physical activity will be assessed using the Paffenbarger Activity Questionnaire (PAQ). Diet will be assessed using a questionnaire assessing frequency of eating behaviors (consuming sugar sweetened beverages, eating fast food) with measurable changes following the use of self-regulation strategies associated with weight outcomes. NRT use. Utilization of NRT will be assessed post-quit through weekly self-report using calendars. Utilization of a fitness app (SR condition only) will be recorded (e.g., number of days for which any dietary tracking occurred) during the weight management portion of the intervention (weeks 1-8).

Intervention outcome effects. Weight: Participants will be weighed in street clothes, without shoes. Weight will be measured at baseline, Quit Day, and post-quit follow-up sessions via an electronic scale. Timeline Follow-Back (TLFB): During each post-quit assessment, participants will be asked to report on smoking since the last assessment. Seven-day point prevalence abstinence will be based on self-report (7 consecutive days of no smoking) and biochemical verification. Exhaled Carbon Monoxide (CO): Alveolar CO will be assessed via the iCOquit® Smokerlyzer® CO ≤6 ppm, to verify self-reported abstinence on Quit Day and at post-quit follow-up sessions.

Process measures. These measures of theoretical processes will be collected at baseline and week 9 to explore effects of treatment on putative mechanisms and subsequent outcome variables. Self-efficacy. Smoking Self-Efficacy Questionnaire (SEQ-12): has two six-item subscales that measure confidence in ability to refrain from smoking when facing internal stimuli (e.g., feeling depressed) and external stimuli (e.g., being with smokers). Weight-efficacy after quitting smoking (WEAQ): is a six-item scale that assesses confidence to prevent weight gain after quitting smoking. Mood. The Positive and Negative Affective Schedule (PANAS): is a 20-item mood inventory with two scales that assess positive and negative affective states. Delay Discounting. Monetary Choice Questionnaire (MCQ): is a 27-item questionnaire that assesses preferences for either a smaller, immediate reward or a larger, delayed reward in order to calculate how quickly a reward diminishes in value as a function of its delayed receipt.

Other measures of interest. Substance use. The timeline followback (TFB) method of assessment to collect data on use of marijuana and other substances. Other measures include: (Modified) Weight Bias Internalization Scale (WBIS), Internalized Stigma of Smoking Inventory (ISSI), Perceptions of Smoking-Related Stigma Scale (PSRSS), Brief Wisconsin Inventory of Smoking Dependence Motives (B-WISDM), Subjective Social Status Ladder (SSS Ladder), Everyday Discrimination Scale (EDS), Brief Self-Control Survey (BSCS), Paffenbarger (Physical Activity) Questionnaire, Self-Weighing Behavior, Eating Away from Home Questionnaire, Health Changes Questionnaire. Utilization of text-based support for quitting will be assessed by determining the number of participants who text "crave" or "slip" and the number of times an individual sends a message with either phrase.

Data Analysis Plan

Feasibility & Acceptability. Average monthly number of individuals screened and enrolled will show feasibility of screening and recruitment. The proportion of participants completing the final study assessment will show feasibility of retention. Response to SR & LE conditions. Attendance. The percentage of treatment sessions attended through week 10 (one week post-quit) will be calculated and compared between conditions; average attendance of ≥70% in both arms suggests good acceptability. Participant Feedback. Participant ratings of intervention satisfaction mean scores ≥3.5 (5-point scale) shows acceptability in each condition.

Intervention effects on treatment outcome variables: Based on ITT principles, all assigned participants will be used in analyses regardless of adherence and missing data. Participants with missing data will be assumed to have smoked and to have regained 0.3 kg/month (positive imputation) and analyses will be repeated using multiple imputation for sensitivity analyses. Generalized estimating equations (GEE) Group x Time analyses will be used for weight change and abstinence. Abstinence. The dependent variable of 7-day point-prevalence abstinence will be analyzed by time (Quit Day, 1, 2, 3-months post-quit) and conditions. Weight. The dependent variable of weight, will be analyzed by time (baseline, Quit Day, 1, 2, 3- months post-quit) and conditions. Secondary exploratory analyses will repeat the GEE analyses adding sex as a variable, and (separately) adding any/no weight loss at week 9 as a variable in predicting smoking abstinence.

Putative mechanisms will be examined using regression analyses to test the effects of treatment on proposed mechanistic variables at week 9, controlling for baseline values. Regression analyses will also test the effects of these proposed mechanisms on follow-up smoking outcomes. Notably, detection of statistically significant effects is not an objective in this limited-powered study.

Confidentiality
Many precautions will be taken to minimize the risk of loss of privacy or confidentiality. The study consent form will inform participants of confidentiality guidelines and standards. Strict confidentiality will be maintained and records will be kept confidential to the level allowed by law. All staff will be trained in procedures for maintaining confidentiality of participant information. Only the investigative team and research staff will have access to non-anonymous records. Personal identifier records will be kept in a locked cabinet or on a secure Brown University computer server, and any forms with identifying information will be stored separately from other study data. Data collection forms will be identified by a unique identification number without personal identifiers. The identifier key will be stored separately from the data collection forms and accessible by the investigative team. Information provided by study participants will not be released to outside sources unless legally required or written consent is provided by the study participant.

D. POSSIBLE RISKS TO PARTICIPANTS, PLAN TO MINIMIZE RISKS, ANTICIPATED BENEFITS OF PARTICIPATION

Potential Risks
Potential risks are minimal and include:
1. Nicotine withdrawal or discomfort following smoking cessation (likelihood high; seriousness low): Upon quitting smoking some individuals experience increases in cravings to smoke, irritability, anxiety, depression, or appetite, changes in sleep, difficulty concentrating, feelings of impatience or restlessness, coughing, dizziness, nausea, or sore throat.

2. Adverse side effects from NRT (likelihood low; seriousness variable): In some individuals, the use of nicotine patch is associated with local skin reactions, mild difficulty sleeping, mild anxiety, (rarely) vivid dreams or nightmares. Local skin reaction in up to 50% of patients, usually mild and self-limiting; rotating patch sites is recommended or discontinuing patch treatment (fewer than 5% of patients). Difficulty sleeping is mild; patients can remove the patch before bedtime and replace it in the morning. The same is true for vivid dreams. Mild anxiety similar to the effects of smoking a few cigarettes is sometimes reported; dosage can be lowered. Common side effects of nicotine lozenges include mouth or throat soreness, indigestion, heartburn, sour or upset stomach, or nausea. These are generally mild and transient. While NRT is intended for use in place of smoking as a smoking cessation aid, some participants may smoke in reduced amounts while using NRT. Research on the effects of using NRT concurrently with cigarette smoking have found no evidence of dangerous consequences of such a practice, including use of up to 42mg of NRT for 2 weeks prior to cessation while continuing to smoke ad libitum. If participants were to smoke while using NRT, they may experience nausea as a side effect.

3. Excessive weight loss or development disordered eating (likelihood low; seriousness moderate to high): A potential risk of participation in a weight loss intervention is losing more weight than would be medically advisable including greater than 20% weight loss from baseline or reaching a BMI $\leq$ 18.5 (underweight). In a previous weight gain prevention study of 599 participants, 1.2% had greater than 20% weight loss from baseline and 0% reached a BMI $\leq$ 18.5. Development of symptoms of disordered eating such as binge eating, excessive food restriction, or compensatory behaviors (e.g., purging, abuse of diet pills or laxatives) as a result of participation in a weight loss intervention is very rare. Previous research has shown that participation in weight loss treatment may actually decrease symptoms of disordered eating such as binge eating and disinhibited eating and does not affect dietary restraint. Similarly, participation in a self-regulation weight loss intervention that utilized daily self-weighing was not

associated with any adverse changes in psychological symptoms including disordered eating behavior. In a previous weight gain prevention study of 599 participants, 0% reported behavior triggering an eating disorder alert.

4. Breach of confidentiality (likelihood low; seriousness variable): One of the potential risks to participants is breach of confidentiality. It is possible that data collection could result in breach of confidentiality.

5. Emotional discomfort from answering questions about physical and emotional health.

Protection Against Risks
Recruitment and Informed Consent. All study procedures will be consistent with the Helsinki Declaration in the protection of Human Subjects. We have made every attempt to minimize risks to participants throughout the study protocol, including loss of privacy or confidentiality, and any potential discomforts. We believe that our planned procedures (described below) will be highly effective for minimizing risk. During initial telephone contact, the nature of the project, the time and risks involved in this study, and inclusion/exclusion criteria will be described. If the potential participant continues to express interest, informed written consent will be obtained. A copy of the consent form will be provided to enrolled participants. The screening protocol will exclude individuals who would be at greater risk as a result of participation in the proposed research. Safeguards to protect against risks will be implemented and maintained throughout each phase of the research study.

Procedures to minimize risk and ensure subject safety:

Medical monitor – Patricia Cioe, Ph.D., R.N.P., has been added to the study as a medical monitor.

1. Nicotine withdrawal or discomfort following smoking cessation (likelihood high; seriousness low): The side effects of nicotine withdrawal are moderately uncomfortable but of minimal risk and with no known medical consequences. NRT patches will be provided to all participants to minimize the severity of any withdrawal symptoms experienced. Patch dose will be dependent upon amount of cigarettes smoked daily and will follow the directions included by the manufacturer. Participants will also be encouraged to use NRT lozenges as needed. They will be encouraged to contact the study team if they experience excessive withdrawal symptoms.

2. Adverse side effects from NRT (likelihood low; seriousness variable): NRT patches and lozenges will be provided to participants who do not have contraindications for use and are medically eligible. Dosing for both products will be dependent upon amount of cigarettes smoked daily and will follow manufacturer recommendations and published criteria. Participants will be counseled on the proper use of NRT before initiating use with ample opportunity to ask questions. Additionally, they will be provided with written material from the National Library of Medicine. This includes information on why NRT is being prescribed, how to use it, precautions for using, possible side effects, storage information, and what to do if they have missed a dose or if they develop certain unwanted symptoms. Participants will be instructed in the proper use of the lozenges. Participants will be advised on potential side effects of smoking while using NRT. Side effects of NRT will be queried during all treatment sessions once use is initiated (3 weeks prior to quitting). Ways to ameliorate side effects (e.g., rotating patch site) will be discussed with participants. Participants will be advised to remove the patch and avoid using other nicotine containing projects if they experience symptoms of nicotine overdose including nausea, vomiting, dizziness, weakness, or rapid heartbeat. They will be asked to call study staff to inform them of their reaction. In these cases, participants will be switched to the next lowest available dose of nicotine patch (i.e., from 21 mg to 14 mg or from 14 mg to 7 mg). Any patient who wishes to discontinue use of NRT will be permitted to do so without penalty.

3. Excessive weight loss or development of disordered eating (likelihood low; seriousness moderate to high): Participants' weight and eating habits will be monitored closely over the course of treatment to minimize the risk of losing more weight than would be medically advisable and for symptoms of disordered eating. Participants reporting past or present diagnosis, treatment, or symptoms of an eating disorder will be excluded from study participation. If a participant has greater than 20% weight loss from baseline or reaches a BMI $\leq$ 18.5 (underweight), the participant will be seen and counseled by a study interventionist. If further weight loss occurs, weight intervention activities will be terminated but the participant will still be eligible for smoking cessation treatment. Participants will be assessed for symptoms of disordered eating using the EDA at weeks 9. If a participant endorses significant symptoms of disordered eating disorder such as binge eating or purging, he or she will be referred to care and all intervention activities discontinued.

4. Breach of confidentiality (likelihood low; seriousness variable): Many precautions will be taken to minimize the risk of loss of privacy or confidentiality. The study consent form will inform participants of confidentiality guidelines and standards. Strict confidentiality will be maintained and records will be kept confidential to the level allowed by law. Only the investigative team and research staff will have access to non-anonymous records. Personal identifier records will be kept in locked cabinets or secure Brown University servers and any forms with identifying information will be stored separately from other study data. Participant data will be identified by a unique identification number without personal identifiers. Information provided by study participants will not be released to outside sources unless legally required or written consent is provided by the study participant.

5. Emotional discomfort. It is possible that participants may experience emotional discomfort when answering some questions. They may choose not to answer any questions and they may stop their participation in the study at any time. They may also request to speak with the PI, a licensed clinical psychologist, at any time if they become upset or experience emotional distress.

Potential Benefits to Participants and Science

Potential benefits include the provision weight management, nicotine replacement therapy, and counseling to quit smoking at no cost to the participants. As a result, participants may lose weight, improve their diet and level of physical activity, and quit smoking resulting in an overall positive impact on their health. Study procedures are carefully developed and followed in order to minimize risks. Given that the risks to subjects are considered to be minimal, the risk-benefit ratio is deemed favorable. Benefits to science and society in general will come from this research project including advancing development of a multiple health behavior change intervention for individuals who are overweight or obese and smoke cigarettes, improving the treatment of nicotine dependence by preventing smoking cessation-related weight gain, and creating research that can be built upon or used for future scientific investigation. By using informed consent procedures, extensively screening for inclusion/exclusion criteria for safety, and by maintaining the confidentiality of records, we significantly reduce risk to our study participants. While we treat the risk of discomfort in our participants with great consideration, and try to minimize it wherever possible by methodological precautions, we feel that these risks are negligible in comparison to the potential benefits of the study.