**Title:** Targeting Maladaptive Eating Behaviors with Mindfulness-Based Training to Prevent Weight Regain

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# Targeting maladaptive eating behaviors with mindfulness-based training to prevent weight regain

## Protocol Summary

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| **Principal Investigator:** | Tanya Halliday |
| **Internal Staff and Sub-Investigators:** | **Site Name** / **Staff Names**<br>University of Utah: Tanya Halliday, Grace Zimmerman, Tanya Halliday, Selene Tobin, Isaac Ou, Victoria Miranda |

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## Background and Introduction

Over 70% of adults in the United States have overweight or obesity (CDC, 2017), which is causally linked to the development and progression of multiple adverse health outcomes (Allison et al., 2008). Weight loss interventions using lifestyle strategies or pharmacotherapy produce clinically meaningful reductions in body mass (Expert Panel, 2014; Magkos et al., 2016). However, due to complex physiological, neuronal and reward-related behavioral process that seek to restore homeostasis(Allison et al., 2008; CDC, 2017; White, Whisenhunt, Williamson, Greenway, & Netemeyer, 2002), maintaining weight loss is challenging and weight regain is common (Hill, Peters, & Wyatt, 2009; Maclean, Bergouignan, Cornier, & Jackman, 2011; MacLean et al., 2015). Due to the high likelihood of weight regain, identification of effective strategies to promote weight maintenance following intentional weight loss is a high priority in the obesity field. Furthermore, it is crucial that interventions be cost-effective and feasibly integrated in to existing health-care systems in order to have a broad impact on the long-term health of US adults. Mindfulness-based interventions are novel approaches that could be well suited for weight loss maintenance due to their success in treating other chronic conditions and behaviors with high relapse susceptibility, such as depression and drug/alcohol addiction (Goldberg et al., 2018). Recently, Dr. Eric Garland (Co-I) demonstrated that his previously developed Mindfulness-Oriented Recovery Enhancement (MORE) intervention(E. Garland, 2013), which has been shown in multiple NIH-funded randomized clinical trials to significantly reduce a range of addictive habits, is effective at reducing maladaptive eating behaviors in adults with obesity (Thomas et al., 2019). MORE is unique from other existing mindfulness based interventions as it combines traditional mindfulness training with cognitive reappraisal and savoring strategies to promote adaptive reward system function. Due to its comprehensive approach and demonstrated therapeutic effects on physiological, neuronal and reward-related mechanisms linked with appetitive behaviors, MORE may be an effective intervention for preventing weight regain. Preliminary data from an ongoing trial in my laboratory with an 8-week mindfulness-based intervention (Halliday & Cornier, unpublished data) indicates that weight regain is minimal (-0.04±1.2% of body weight) and that participants (n=7) report high satisfaction (average sores >9 out of 10 for content and weight-loss maintenance) with the intervention. However, to date, no randomized trial has evaluated the efficacy of MORE for preventing weight regain, nor have the long-term effects of mindfulness-based interventions on weight loss maintenance been investigated.

## Purpose and Objectives

The overall objective of this study is to evaluate the effectiveness of a mindfulness-based intervention to prevent weight regain in weight-reduced adults.

A secondary objective is to perform preliminary efficacy testing comparing the impact of MORE vs standard weight loss maintenance advice (CON) on weight loss maintenance and eating-related behaviors (disinhibition, hedonic hunger, food cravings, and ad libitum energy intake).

To meet these objectives, we propose the following aims:

**Specific Aim 1: Determine the effect of MORE on weight loss maintenance.**

**Hypothesis:** MORE will result in less weight regain compared to CON after the 8-week intervention, and benefits will be sustained in a 6-month follow-up.

**Specific Aim 2: Determine the effect of MORE on reward-related behavioral processes (e.g., food cravings) and ad libitum energy intake.**

**Hypothesis:** MORE group will demonstrate changes in eating behaviors and energy intake associated with preventing weight regain compared to CON immediately after MORE and after 6-months of follow-up.

## Study Population

**Age of Participants:** 18-65

**Sample Size:**
At Utah:
All Centers: 100

**Inclusion Criteria:**
We will enroll the following three subgroups (ages 18-65 years):

- Lifestyle weight loss: weight loss of 7% body mass via intentional weight loss within past 6 months; BMI >25 kg/$m^2$ prior to intentional weight loss.
- Medical weight loss patients: patients of the bariatric weight loss clinic, weight loss of 7% body mass via intentional weight loss within past 6 months; BMI >25 kg/$m^2$ prior to intentional weight loss; stable for 3 months on medications.
- Bariatric Surgery patients: 12-20 months post-operation.

**Exclusion Criteria:**
Exclusion Criteria: uncontrolled cardiovascular, metabolic, renal, or pulmonary disease; cancer treatment in past 5 years; untreated thyroid disease or other medical condition affecting weight or energy metabolism; severe food allergies; women who are pregnant, lactating, or planning pregnancy during participation in the trial; active psychiatric issues. Scheduled bariatric surgery within the next 6 months. No access to WiFi at residence. No access to a smart device as a personal device (with access to applications). Complete hearing loss.

Additional criteria specific to patients with a history of bariatric surgery: <12 months post-op; weight regain of >5% of body mass post-operation; history of admittance to rehabilitation facility; history of post-op complications that require recent inpatient management; patients who were required to stay in the hospital >1 week post-op; revision surgery patients; heart failure patients.

Additional criteria specific to lifestyle and medical weight loss participants: Bariatric surgery within the past 2 years

## Design

Randomized Trial

## Study Procedures

**Recruitment/Participant Identification Process:**

- **Chart Review**
  - Participants will be recruited from the Electronic Health Record (EHR) in the UU Health system. Participants meeting initial criteria will be contacted via email or opt-out letter, inviting them to complete a medical history screening survey over the phone with a member of the research team to further determine eligibility. We will also recruit via passive techniques (i.e. fliers in campus, clinics, and community locations; newspaper and social media ads).
- **Referral**
  - Physicians at University of Utah Health primary care clinics will be able to refer eligible patients from their clinical practice to the study. Clinics will either be provided with a simple referral form that patients can complete if interested.
  - Surgeons at The Bariatric Surgery clinic at University of Utah will also refer patients to this study. A Study coordinator will be in clinic to provide study information and enroll referred patients who may be interested in participating.
- **Flyers**
  - Flyers will be placed on campus and in community centers. Flyers will also be sent out electronically via University of Utah email lists. Advertisement flyers will also be posted on relevant University of Utah research-related websites.
- **Follow-Up**
  - PI or research assistant will follow up via phone or email (using the selene.tobin@utah.edu account) once an individual has expressed interest in the study from one of the recruitment techniques. No more than 3 contact attempts will be made.

**Informed Consent:**

**Description of location(s) where consent will be obtained:**

Consent will be obtained in: - a private room in the HPR complex - a private room in the Bariatric Surgery Clinic - over a private HIPPA compliant Zoom session (e-consent)

**Description of the consent process(es), including the timing of consent:**

Informed Consent will be completed in person, or over a private HIPAA compliant Zoom call, with a member of the study team and the potential participant. During the explanation of the consent form and after the study team member goes over the details of the Informed Consent document, the potential participant will be given a chance to ask questions regarding study procedures. The study team member will assess understanding of the consent form and study procedures by asking the potential participant to briefly recite back study-related commitments and procedures. Potential participants will be told that they are free to take the consent form home with them and decide to sign it and participate in the study at a later time if they are uncomfortable with consenting to the study during this visit. In addition, to provide participants with greater time between seeing the consent form and signing it, the consent form will be emailed to participants, and available to them via REDcap, prior to the screening visit so that they can view it on their own time 1-year follow-up visit addition to study: As of March 2023, participant enrollment will be over. At that time, participants who are still in

ongoing data collection (have not completed the six month follow up visit), will be contacted and asked to sign a new consent document ("Informed Consent Document_v.03.13.23_Clean") that outlines one additional contact event at 1 year (6 months following the 6 month study visit). At this time, participants who have formally completed their data collection (have completed the six-month follow-up visit), will be contacted via email (2 contact attempts) and phone (1 contact attempt; for a total of 3 contact attempts) and will be asked if they have interest in enrolling in the study for the 1 year follow up contact event. These participants will be provided a copy of the consent document they previously signed, and they will be provided a new consent document outlining this additional study event (One Year Follow-up Informed Consent Document_v.03.13.23_Clean). If they would like to participate in the 1 year follow up they will be asked to sign the new consent document. These specific changes are being done so that participants who are currently enrolled in the study can simply sign an updated consent document to participate in the 1 year follow up event. And participants who are no longer in contract with the original informed consent document can opt-in to this new study event with a simplified consent document. All processes followed in obtaining the initial consent that are explained above will be followed.

## Procedures:

**PRE-SCREENING:** Subjects who are interested in participating with undergo a pre-screening in which they will answer questions over Redcap, or via a phone screening with trained study staff, about their medical history and they will be assessed on all inclusion and exclusion criteria.

**SCREENING:** After pre-screening, interested participants that remain eligible will be scheduled for a Zoom screening visit to determine eligibility. After providing written informed consent, participants of childbearing potential will perform a pregnancy test that will be delivered to their home. Upon completion of a pregnancy test participants will be asked to report the results over Zoom. Participants will also be asked to remotely complete the EATS-26 questionnaire (Garner, Olmsted, Bohr, & Garfinkel, 1982) to screen for eating disorder risk, The Patient Health Questionnaire 9-Item (PHQ-9)(Kroenke, Spitzer, & Williams, 2001) to screen for depression, and the Alcohol Use Disorders Identification Test (AUDIT)(Daeppen, Yersin, Landry, Pécoud, & Decrey, 2000) to screen for alcohol use disorders via REDcap. Participants that remain eligible and are willing to participate in the trial will complete the following assessments:

**BASELINE TESTING:**

- **Body Mass, Height, and Composition** via digital scale, stadiometer, and BodPod (air displacement plethysmography)
- **Validated Eating-Related Behavioral Questionnaires** to assess dietary restraint, disinhibition and hunger (Three Factor Eating Questionnaire); diet-specific self-efficacy (Weight Efficacy Lifestyle Questionnaire); and food cravings (Food Craving Inventory; FCI); Interoceptive Awareness (Multidimensional Assessment of Interoceptive Awareness; MAIA); and savoring (Ways of Savoring Checklist)
- **Free-living Energy Intake (EI)** via automated 24-hr dietary recall (ASA-24) administered online through the Clinical Services Core of the CCTS. This recall will be administered on 3 non-consecutive days,including 2 weekdays and 1 weekend day.
- **Meal Test:** Participants will also complete a baseline meal test visit for assessment of appetite-related markers. Participants will be asked to keep a 1-day food log the day before this testing visit at baseline and asked to repeat this same meal pattern the day before the post-intervention testing visit. Participants will present to the Human Performance Laboratory in the morning after an overnight fast and having refrained from exercise for the prior 48-hours. Participants will next consume a standard breakfast meal (25% of the total energy needs). Repeat appetite evaluations will be performed at 30, 60, 90, 120, 150, and 180 minutes post-meal. Participants will then be offered a buffet-style lunch to measure *ad libitum* energy intake

- **Randomization:** Following enrollment and completion of baseline testing a randomization assignment will be generated by computer and block randomization will be performed within strata defined by sex. Participants will be randomized 1:1 to MORE or CON

**INTERVENTION:**

**Group-Based Interventions**

- **MORE:** Participants randomized to MORE will complete the previously developed 8-week, MORE program (E. Garland, 2013). MORE is delivered in a group format, consisting of 8 weekly HIPPA compliant virtual zoom 2-hour sessions. The MORE curriculum will be adapted for this intervention to address food intake behaviors and will provide training in mindfulness techniques to increase awareness of, and self-control over, cravings; reappraisal skills to promote emotion regulation and restructure motivations for highly palatable food intake; and savoring pleasant events and emotions to overcome defects in natural reward processing. In addition to class sessions, participants will complete daily, 15-minute, audio-guided mindfulness, reappraisal, and savoring sessions at home. The intervention will be delivered by a study team member who will receive training and supervision from Dr. Garland. Treatment fidelity will be monitored as in ongoing RCTs of MORE (E. L. Garland, Manusov, et al., 2014).
- **CON:** Participants randomized to the control intervention will complete an 8-week healthful lifestyle program via HIPPA compliant zoom sessions. The curriculum will be based on the Diabetes Prevention Program's Prevent T2 for Life program, which is an evidence-based national healthful lifestyle maintenance intervention. This program includes training in healthful eating, meal planning, and recipe modification; time and stress management; adapting lifestyle habits for continued success during holidays, vacations, and other special situations; and relapse prevention. CON will be virtually delivered by a study team member who will receive training and oversight from Dr. Halliday, who has delivered this intervention previously. In addition to class sessions, participants will be completed daily, 15-minute activities related to the course content (i.e. – designing a meal plan and grocery shopping list; creating a list of healthful take-out or restaurant meals; etc) at home. Time-in-treatment will be matched between conditions.

**POST-INTERVENTION TESTING:** Repeat baseline testing at the end of 8 weeks and at 6 months.

OPTIONAL POST-INTERVENTION TESTING AT 1 YEAR: 6 months after the post-intervention testing time point participants will be contacted and asked to complete follow-up questionnaires. These questionnaires are designed to assess participants' perceptions of the intervention and if they achieved their weight-loss maintenance goals.

**STOPPING PROCEDURES and ADVERSE EVENTS**: Participants will be encouraged to report any adverse events that they believe may have been a result of the study.

**Procedures performed for research purposes only:**

## Statistical Methods, Data Analysis and Interpretation

The statistical analysis plan presented below was developed in collaboration with Dr. Jincheng Shen of the SDBC.

**Aim 1** will focus on the efficacy of the intervention (MORE vs. CON) on the primary outcome of body mass and body composition at week 8 and week 24. We will first provide descriptive summaries of each variable measured at week 0 (baseline), week 8 and 24, as well as by intervention group. Linear mixed models (LMM) will then be used to relate weekly assessments of body mass from week 0 to week 24 to the intervention, controlling for covariates likely to be associated with the outcome. Specifically, this will include baseline body mass and composition, and other demographic covariates including (but not be limited to) age, sex, race and socioeconomic status. Different slopes for time trend and intervention-time interaction term will be assumed for the intervention period (week 0-8) and follow-up period (week 8-24). Random intercepts will be used to account for correlations on the participant level. An advantage of this approach is treatment effect estimates remain consistent and approximately unbiased if missing data follow a missing-at-random pattern (MAR; data values are independent of missingness mechanism conditional on the observed data), the most general data-centric missing data assumption. Secondary analyses will fit separate LMM models to assess changes in fat mass and lean mass measured at week 0, 8 and 24. Similarly, LMM will be fitted for each of the eating behaviors and energy intake outcome collected for **Aim 2** (detailed above), where skewed outcomes may be transformed to approximate normality. Bonferroni correction will be performed to adjust for multiple comparisons.

Sample size, and power consideration: For a total of 100 participants randomized 1:1 to each study arm, we conservatively anticipate 20% attrition. This leaves us with complete data on n=80 participants total (n=40 per group). This provides ≥80% power for detecting differences in body mass (or other outcomes assessed in Aim 1 and 2) by at least 0.89 standard deviations. We expect power will be greater for our primary analysis models when adjusting for covariates associated with outcomes. Although we will have limited statistical power for the current analysis this trial will generate the effect size necessary to power a future trial, while allowing us to collect outcome measures on a practical amount of participants within the 2-year award period.