Science of Behavior Change (SOBC)

Applying Novel Technologies and Methods to Inform the Ontology of Self-Regulation

Aim 2 Non-lab Study Protocol

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Introduction

Health risk behavior, including poor diet, physical inactivity, tobacco and other substance use, causes as much as 40% of the illness, suffering, and early death related to chronic diseases. Non-adherence to medical regimens is an important exemplar of the challenges in changing health behavior and its associated impact on health outcomes. Although an array of interventions has been shown to be effective in promoting initiation and maintenance of health behavior change, the mechanisms by which they actually work are infrequently systematically examined. One promising domain of mechanisms to be examined across many populations and types of health behavior is of self-regulation. Self-regulation involves identifying one's goals, and maintaining goal-directed behavior. A large scientific literature has identified the role of self-regulation as a potential causal mechanism in promoting health behavior.

Advances in digital technologies have created unprecedented opportunities to assess and modify self-regulation and health behavior. In this project, we plan to use a systematic, empirical process to integrate concepts across the divergent self-regulation literatures to identify putative mechanisms of behavior change to develop an overarching "ontology" of self-regulatory processes.

This multi-year, multi-institution project aims to identify an array of putative psychological and behavioral targets within the self-regulation domain implicated in medical regimen adherence and health behavior. This is in service of developing an "ontology" of self- regulation that will provide structure and integrate concepts across diverse literatures. We aim to examine the relationship between various constructs within the self-regulation domain, the relationship among measures and constructs across multiple levels of analysis, and the extent to which these patterns transcend population and context. The project consists of four primary aims:

Aim 1. Identify an array of putative targets within the self-regulation domain implicated in medical regimen adherence and health behavior across these 3 levels of analysis. We will build on Multiple PI Poldrack's pioneering "Cognitive Atlas" ontology to integrate concepts across divergent literatures to develop an "ontology" of self-regulatory processes. Our expert team will catalog tasks in the self-regulation literature, implement tasks via online testing (Mechanical Turk) to rapidly obtain large datasets of self-regulatory function,

assess the initial ontology via confirmatory factor analysis and structural equation modeling, and assess and revise the resulting ontology according to neural similarity patterns across tasks (to identify tasks for Aim 2).

Aim 2. Evaluate the extent to which we can engage and manipulate putative targets within the self-regulation domain both within and outside of laboratory settings. Fifty smokers and 50 overweight/obese persons with binge eating disorder will participate in a lab study (led by Poldrack) to complete the tasks identified under Aim 1. We will experimentally modulate engagement of targets (e.g., stimulus set of highly palatable foods images or tobacco-related images as well as self-regulation interventions). A comparable sampling of 100 persons will participate in a non-lab study (led by Multiple PI Marsch) in which we will leverage our novel mobile-based behavioral assessment/intervention platform to modulate target engagement and collect data in real-world conditions.

Aim 3. Identify or develop measures and methods to permit verification of target engagement within the self-regulation domain. Led by Co-I MacKinnon, we will examine cross-assay validity and cross-context and cross-sample reliability of assays. We will employ discriminant and divergent validation methods and Bayesian modeling to refine an empirically-based ontology of self-regulatory targets (to be used in Aim 4).

Aim 4. We will evaluate the degree to which engaging targets produces a desired change in medical regimen adherence (across 4 week interventions) and health behavior among smokers (n=100) and overweight/obese persons with binge eating disorder (n=100) (objectively measured smoking in the former sample and exercise in the latter sample). We will employ our novel mobile behavioral assessment/intervention platform to engage targets in these samples, given that (1) it offers self-regulation assessment and behavior change tools via an integrated platform to a wide array of populations, and (2) content within the platform can be quickly modified as needed to better impact targets. The proposed project is designed to identify valid and replicable assays of mechanisms of self-regulation across populations to inform an ontology of self-regulation that can ultimately inform development of health behavior interventions of maximal efficacy and potency.

This protocol details the Aim 2 non-lab study led by Multiple PI Marsch.

Objective

Evaluate the extent to which we can engage and manipulate putative targets within the self-regulation domain outside of laboratory settings in samples of smokers and overweight/obese individuals with binge eating disorder. Fifty smokers and 50 overweight/obese individuals with binge eating disorder will be recruited to participate in a non-lab experimental paradigm (led by Multiple PI Marsch) in which we will leverage our novel mobile behavioral assessment/intervention technology platform. We will measure and modulate engagement of potential self-regulation targets and collect data in real time and in real-world conditions. Up to an additional 50 participants will have mobile sensing added to the design. (We plan to over-recruit to produce the desired analytic sample sizes.)

Study Design

This phase of the study takes what we learned about self-regulation in the first phase and tests it in two samples that are exemplary for "lapses" in self-regulation: individuals who smoke and overweight/obese individuals with binge eating disorder. We expect that many real-world conditions (e.g., temptation, negative affect) may decrease self-regulation, whereas training through the mobile intervention described below may increase self-regulation. The primary purpose of this study is to determine whether we can shift self-regulation for the ultimate goal (in Aim 4) of targeting self-regulation to impact health behaviors.

Based on information provided in the study ads, interested individuals will be directed to an eligibility screening questionnaire through Dartmouth's Research Electronic Data Capture (REDCap) system and may call or email our study staff with questions. Those who meet the eligibility criteria for the study based on the online screening will be verified by phone and then scheduled for a study period of 14 consecutive days, with no in-person visit necessary. Those in the EMA-plus-mobile-sensing samples will be scheduled for an in-person intake. The study staff will determine (online for the EMA-only participants; in person for the EMA-plus-mobile-sensing participants) whether possible participants are willing to consent to the study, and participants who consent will sign a consent form (electronic through REDCap via a checkbox or "agree" button) and be offered an electronic or paper copy. Consenting participants will complete baseline questionnaires, including demographics and the self-regulation questionnaires from which

momentary self-regulation questions were adapted (as described in the assessments below). The EMA-plus-mobile-sensing participants will have an in-person intake to be given, and be trained on the use of, a study-provided smartphone and three study-provided wrist sensors. EMA-only participants will use their own smartphones and will not be asked to wear wrist sensors. We expect the baseline assessments to take approximately 30 minutes of participants' time and for the EMA-plus-mobile-sensing participants' device training to take approximately an additional 30 minutes of their time.

During the study period (the details of which are below), participants will complete an assessment battery of putative targets of self-regulatory function, consisting of a subset of the questionnaires used in the Aim 1 MTurk phase, with specific self-regulation questions further refined at a momentary level through a pilot study. Participants will be asked to complete items in response to queries using mobile ecological momentary assessment (EMA); i.e., questions/questionnaires asked at a given time point outside of a laboratory setting via a mobile device. We will assess antecedent conditions prior to health risk behavior: smoking or binge eating among our smoking and binge eating samples, respectively. These antecedent conditions include mood, companionship, location, and temptation. This will allow us to better understand real-world conditions that may engage and modulate putative targets of self-regulatory function in undesired directions. We will offer the resources of Laddr® (a science-based behavior change intervention delivered via an interactive, self-directed mobile platform) to individuals and assess the effect of this mobile intervention system on putative targets of self-regulatory function. Laddr will also be used to deliver the EMAs to participants.

For a set of additional participants, we will add mobile sensing to capture data to infer physical activity, sleep, stress, smoking, and eating behavior. EMA-plus-mobile-sensing participants will carry a study-provided Android smartphone and wear two study-provided wrist sensors (one on each wrist) to facilitate the collection of these additional data, which will both add information we are not collecting via EMA and help to validate the information we are collecting via EMA. EMA-plus-mobile-sensing participants will be provided a third wrist sensor to wear at night while the daytime wrist sensors are charging. This mobile sensing component will be conducted in collaboration with Dr. Santosh Kumar at the University of Memphis, who has a wealth of experience in the field and has

pioneered much of the work in mobile sensing, as well as his colleagues (Drs. Emre Ertin at Ohio State University and Mustafa al'Absi at the University of Minnesota). All three of these researchers are part of the Center of Excellence for Mobile Sensor Data-to-Knowledge (MD2K). Additionally, the mobile sensing data will be collected via mCerebrum, a mobile application developed by our colleagues at MD2K.

We will ask participants to respond to EMAs and to engage with the mobile intervention for 14 consecutive days. We will prompt them four times daily to inquire about health risk behavior and ask them to complete measures of putative targets. We will send the four prompts at random times within time windows (e.g., 8-11:30 AM, 11:30 AM – 3 PM, 3-6:30 PM, 6:30-10 PM). The time windows may vary based on participants' waking hours, and we will program through the software at least an hour between prompts (e.g., if a participant receives a prompt at 11 AM, he/she cannot receive another prompt until 12 PM). We will ask them to use Laddr daily to, at a minimum, update progress toward goals and complete various activities on the application that we expect will improve their self-regulation. Participants will be recommended priority therapy guides (binge eating for the binge eating sample; smoking for the smoking sample) and can also choose to engage with other guides, such as depression, anxiety, and substance use.

With the exception of charging, wearing, and leaving the wrist sensors turned on, EMA-plus-mobile-sensing participants will not be required to engage with the mobile sensing components, which will collect data automatically (passively).

All participants will be asked to complete a brief follow-up survey at the end of their two-week study period. EMA-only participants will be compensated in full at the end of their study period via an Amazon gift card (primary option) or a check. If participants request a check, they will be required to give their legal name, legal mailing address, and Social Security number. EMA-plus-mobile-sensing participants will revisit our research center in person to return the smartphones and wrist sensors and receive cash with their full compensation for the entire study period.

Samples

This study consists of samples from two target populations: (1) persons who

smoke, and (2) overweight/obese persons with binge eating disorder. The specific eligibility criteria are as follows:

Inclusion criteria:

- Age 21-50 years
- Understand English sufficiently to provide informed consent
- Use a smartphone (EMA-only participants); proficient with using smartphone and comfort wearing devices (EMA-plus-mobile-sensing participants)

- **Additional inclusion criteria for binge eating sample:**
  - $27 \leq BMI \leq 45$ kg/m^2
  - Have binge eating disorder according to DSM-5 criteria
  - Non-smoking (defined as no cigarettes in past 12 months—this includes former and never smokers)

- **Additional inclusion criteria for smoking sample:**
  - Smoke 5 or more tobacco cigarettes/day for past year
  - $17 \leq BMI < 27$ kg/m^2

Exclusion criteria:

- Any current substance use disorder
  - Will not exclude based on use of substances
- Currently pregnant or plans to become pregnant in next 3 months
- Lifetime history of major psychotic disorders (including schizophrenia and bipolar disorder)
- Current use of any medication for psychiatric reasons (including stimulants and mood stabilizers)
- Current use of prescription pain medications (e.g., Vicodin, oxycodone)
- Current use of any medication for smoking
  - Exceptions: short-acting NRT (e.g., gum, lozenge, nasal spray, inhaler)
  - Will screen out for Wellbutrin or varenicline
- Current use of any medication for weight loss
- Have undergone weight-loss surgery (e.g., gastric bypass, lap band)
- Current nighttime shift work or obstructive sleep apnea
- NOTE: We will not exclude based on e-cigarette use.

- **Additional exclusion criteria for binge eating sample:**
    - Compensatory behavior (e.g., purging, excessive exercise, fasting)
        - Already excluded as part of the DSM-5 binge eating disorder criteria
    - Lost weight in recent past (>10 pounds in past 6 months)
    - Currently in a weight-loss program (e.g., Weight Watchers, Jenny Craig)
        - Ask about, but won't exclude on, online/mobile app weight-loss programs as part of the screener
    - Currently on a special diet for a serious health condition

- **Additional exclusion criteria for smoking sample:**
    - Binge eating behavior according to QEWP-5 ("yes" to questions 8 and 9 and for question 10, at least one episode per week for three months).
        - QEWP-5 #8: During the past three months, did you ever eat in a short period of time (for example, a two-hour period) what most people would think was an unusually large amount of food? [yes or no]
        - QEWP-5 #9: During the times when you ate an unusually large amount of food, did you ever feel you could not stop eating or control what or how much you were eating? [yes or no]
        - QEWP-5 #10: During the past three months, how often, on average, did you have episodes like this? That is, eating large amounts of food plus the feeling that your eating was out of control? (There may have been some weeks when this did not happen. Just average those in.) [less than one episode per week, five response options for 1 or more episodes per week]

Recruitment

Study advertisements will be posted online (e.g., Craigslist, Facebook) as well as placed in physical locations in the Dartmouth community around New Hampshire and Vermont, including Dartmouth-Hitchcock Medical Center (DHMC) and other health centers and frequented places in the community (e.g., gas stations, buses). Our team has had great success with similar recruitment strategies in decades of research studies. We expect the national sample of EMA-only participants to

include approximately 50% women, 23% non-White race, and 18% Hispanic, and the local sample of EMA-plus-mobile-sensing participants to include 50% women, 5% non-White race, and 1% Hispanic.

Compensation

As this is not an "intent-to-treat" sample where adherence to the intervention itself is an important outcome to study, compensating participants for active study participation will help ensure exposure to the intervention intended to manipulate targets.

EMA-only participants will be compensated according to the following schedule:

$20 per participant for all baseline surveys (required to complete full battery of surveys to receive $20)

*$1 per EMA * 4 EMAs per day * 14 days = up to $56*

*$2 per day for Laddr activities (at least 5 minutes of engagement) * 14 days = up to $28*

*$20 bonus per week for completing minimum of 25 EMAS (~90% of 28 total EMAs in the seven-day period) * 2 weeks = up to $40*

$31 for data plan reimbursement (required to complete minimum of 6 EMAs)

Total: up to $175 over two-week study period

EMA-plus-mobile-sensing participants will be compensated according to the following schedule:

$20 per participant for in-person training and all baseline surveys (required to complete full battery of surveys to receive $20)

*$1 per EMA * 4 EMAs per day * 14 days = up to $56*

*$2 per day for Laddr activities (at least 5 minutes of engagement) * 14 days*

= up to $28

*$4 per day for carrying phone and properly wearing wrist sensors for at least 18 hours per day * 14 days = up to $56*

*$20 bonus per week for completing minimum of 25 EMAS (~90% of 28 total EMAs in the seven-day period) * 2 weeks = up to $40*

$25 for returning smartphone

$25 for returning all three wrist sensors

Total: up to $250 over two-week study period

Note that these schedules are based on the maximum compensation possible. Participants may receive partial compensation for certain activities, such as partial completion of Laddr activities in a given week. EMA-plus-mobile-sensing participants may receive a deduction in compensation for lost or damaged study phones or wrist sensors. Participants will be compensated with their full payment at the end of their study period.

Study Assessments

Baseline

- Demographics
- Reward-based Eating Drive Scale (RED-13)
- Fagerström Test for Nicotine Dependence [Smoking Sample Only]
- Short Self-Regulation Questionnaire (SSRQ)
- Emotion Regulation Questionnaire (ERQ)
- Five Facet Mindfulness Questionnaire (FFMQ)
- Mindful Attention Awareness Scale (MAAS)
- Selection-Optimization-Compensation (SOC) Questionnaire – Short Version
- UPPS-P Impulsive Behavior Scale – Lack of Premeditation and Lack of Perseverance Subscales
- Eysenck I-7 Impulsivity and Venturesomeness Questionnaire – Venturesomeness Subscale

EMA

- Momentary self-regulation questionnaire
- Self-reported behavior of interest (binge eating for the binge eating sample; smoking for the smoking sample)
- Questions assessing intent
- Questions assessing contexts

Follow-up

- Is there anything that happened during the two-week period that influenced the quality of the information you were able to provide or your ability to participate in the study? If yes, please describe.
- Do you have any other comments you would like to share?

Data Monitoring

The research assistant plans to monitor data quality on a daily basis and report any issues to the project manager and senior data manager. Our study team will use an initiation application for Laddr, developed by the same team that developed Laddr, to initiate participants into the EMA portion of the study. The team will download password-protected raw data files from a website created by the Laddr developers to monitor EMA completion and Laddr usage. These files will also allow the study team to track compensation amounts for each participant. Data are uploaded to the server when the smartphone is connected to the Internet (either via cellular or WiFi). If participants do not have access to a connection, the data are stored locally on the smartphone and uploaded to the server once a connection is established. Poor compliance will first be addressed through reminders sent to the participant's smartphone or email address. If poor study compliance persists, the participant may be withdrawn from the study, and an additional participant will be enrolled.

For the EMA-plus-mobile-sensing participants, our study team will use the MD2K infrastructure (mCerebrum, the mobile sensing application, and Cerebral Cortex, the big data companion to mCerebrum that allows for data analysis and visualization). The MD2K software automatically detects the amount of time that participants have worn the wrist sensors, and as long as participants maintain a wireless connection (either cellular or WiFi), the sensor data are uploaded to the MD2K server every 15 minutes, allowing for monitoring throughout the day. If

participants do not have access to a connection, the data are stored locally on the smartphone and uploaded to the server once a connection is established. Cerebral Cortex allows for real-time data monitoring. Poor compliance will first be addressed through reminders sent to the participant's study smartphone or email address. If poor study compliance persists, the EMA-plus-mobile-sensing participant may be withdrawn from the study, and an additional participant will be enrolled.

Sample Size and Justification

For the EMA-only study, we propose a sample size of up to 200 participants (100 individuals who smoke and 100 overweight/obese individuals with binge eating disorder) recruited from the United States, including U.S. districts and territories. Up to 100 additional participants (50 individuals who smoke and 50 overweight/obese individuals with binge eating disorder) will be recruited from the Dartmouth area and surrounding communities to add mobile sensing to the design.

We propose the sample sizes above to reach EMA-only analytic samples of 50 participants each for smoking and binge eating, and EMA-plus-mobile-sensing analytic samples of up to 25 participants each for smoking and binge eating. The proposed sample sizes account for participants who sign consent but participate minimally.

With 50 participants per sample, each with multiple assessments per day, the sample size for such analyses will be adequate to model these processes. While calculating exact detectable effect sizes will depend on several as yet determined factors (standard deviation [SD] of self-regulation measures, proportion of signals in challenging versus not challenging contexts, response rate, intraclass correlation of EMA responses within individual), we estimate 80% power to detect a difference between contexts in mean self-regulation target value that is 0.2-0.3 times a SD. This assumes 2 signals/day for 2 weeks at an 80% signal response rate, with intraclass correlations ranging from 0.001 to 0.3, and for both 10% and 30% challenging context prevalence at signal time.

The EMA-plus-mobile-sensing sample size will allow for exploratory analyses that add mobile sensing data to the EMA data.

Statistical Analysis Plan

Multi-level models are planned to assess the relationship between self-reported context and behaviors and target measures collected via EMA. We will add passively sensed measures as additional predictor features into models assessing main effects and interaction with the Laddr intervention. The intensity of data collection via both EMA and passive sensing allows modeling of the dynamic processes involved in self-regulation. That is, we expect real-world context to influence self-regulation targets in real-time. Likewise, the influence of challenging real-world contexts on unhealthy behavior may change in response to interventions aimed at influencing these targets. Passively sensed behavior will be added as real-world contexts to be considered in these models. EMA and passive sensing allows the temporal evaluation necessary to evaluate this process. We can examine in-the-moment relationships between unhealthy behaviors and target self-regulation measures. In addition, we can examine how immediate contextual and environmental factors influence both measures of self-regulation and unhealthy behaviors. We can also assess how these relationships change over time in response to use of the mobile intervention modules. EMA and passive sensing data are necessary for modeling these fine-grained, dynamic processes, as effect of real-world stimuli on putative self-regulatory targets are expected on a momentary basis. Some of the planned mechanistic modeling will be performed via structural equation models (SEM) which can incorporate both complex relationships between variables (such as mediation) and latent variables measured with error. As self-regulation will be measured via multiple self-reported items on the EMA, it can be considered a latent construct in the mechanistic models. Likewise, now having both self-report and behaviorally sensed information about the behavior will allow us to better model the true, unobserved unhealthy behavior as a latent variable in the relationship between context, behavior, and self-regulation, increasing the accuracy of the estimates of the relationships.

The planned flexible spline models that examine patterns of target measures around smoking and eating will be performed on all events whether detected via self-report or behaviorally sensed. This will allow us to both examine patterns of self-regulation around events (previously planned), but will also allow us to determine whether this pattern differs when the event was reported versus not reported. Additionally, a validation of self-reported smoking instances will be performed, as smoking can be passively sensed via the wristband. A similar

validation of instances of eating is also possible. Precision and recall percentages can be generated for each mode of data collection (passively sensed and self-report) using the other as ground truth. It is likely that both modes represent measurement of true behavior with error and such validation exploration will inform future data collection in each mode. Finally, we will analyze participant behavior during times of non-response to the active EMA data collection and explore how these behavioral patterns are distinct from times when participants are responding. We aim to better understand which behaviors and contexts are related to non-response and self-regulation. This will be accomplished in two steps. First, behavioral features will be entered into machine learning algorithms trained on the labeled observations when both self-report and sensor data is available with the goal of predicting self-reported self-regulation measures. Next, the resultant optimal model will be used to predict the values of self-regulation measures during the spans of time when participants do not self-report target measures. If the predicted target measures during the non-responsive times are significantly different than those when the participant is responsive, this would further validate the target as a measure of self-regulation as disengagement from Laddr and data collection are likely related to self-regulation.

Protection of Human Participants

Potential Risks:

The potential risks associated with the data collected are low.

Risks from behavioral testing: The types of data we plan to collect (assessment, self-report questionnaires, behavioral testing) will not harm the participants' financial standing, employability, or reputation, or expose the participant to civil or criminal liability. The types of risk associated with the data collected include possible fatigue, frustration, or the discussion of sensitive or personal information. If participants do not wish to answer any questions, they may elect not to do so, and may continue in the remainder of the study without penalty. Additionally, participants may be concerned about confidentiality risk when using the Internet to access Laddr, even on secured, encrypted connections. They may also be worried about prompts they receive on a mobile device designed to remind them to complete Laddr activities, such as updating goals.

Risks from mobile sensing (EMA-plus-mobile-sensing participants only): This project does not involve any risks beyond those ordinarily encountered in daily life or the performance of routine tests. Participants may experience slight initial discomfort while wearing the wrist sensors, such as minor skin irritations. As with any electrical device, the sensors can theoretically cause electric shocks. Electrical shocks can be a health concern with certain health conditions (e.g., heart conditions that require a pacemaker). Additionally, participants could have privacy concerns regarding mobile sensing.

Risks from electronic databases: There may be risks to participants by virtue of their representation in electronic databases, principally involving the risk that privacy or confidentiality might be compromised if there were lapses in security of the information contained in these databases.

Adequacy of Protection Against Risks

A. Informed Consent:

All descriptions in the informed consent form are written at the 8th grade reading level. The consent document includes descriptions about: background of the study, study procedures, risks and discomforts, benefits, payment for participation, voluntary nature of participation, privacy and confidentiality, and contact information for the research team. The consent form will be presented to prospective primary study participants online and to prospective pilot study participants in person.

Individuals who wish to participate in the study will be asked to carefully read the consent form or to have the consent form read to them. If they have any questions about the study, they can ask the study staff before consenting and at any time afterward. Individuals who provide consent for participation in the study will be offered an electronic or paper copy of the form. Their screening information, agreement to participate, contact information, and baseline data will be saved in REDCap. Study participants will be informed that they can withdraw from the study for any reason at any time.

Prior to giving informed consent, EMA-plus-mobile-sensing participants will be invited to try on the wrist sensors in order to factor device comfort into their consent decisions.

EMA-plus-mobile-sensing participants may be asked to provide government-issued photo identification before enrolling to verify age and identity, and their request to enroll may be declined if they are unwilling or unable to provide this identification.

B. Protections Against Risk:

Protection against risks from behavioral testing: To protect against the possible risks associated with behavioral testing, which are fatigue and frustration, participants will receive EMA prompts four times daily and will not be asked to initiate use on their own. It will be made clear to participants during the informed consent process that they are free to discontinue their participation at any point without penalty. Any participant that experiences significant discomfort during the two-week period will be able to stop procedures immediately.

To protect against concerns that others may see when a participant receives a prompt from the Laddr system (the mobile behavior change intervention), the content of the prompts sent will be intentionally vague. While they will be designed to be meaningful to individual participants, they will not include specific references to study participation.

Protection against risks from mobile sensing (EMA-plus-mobile-sensing participants only): Previous studies with wristband sensors have indicated that after a brief adjustment period, the majority of the participants adjusted to wearing the bands and did not find them to be intrusive or restraining. Although slight discomfort is possible from wearing the wrist sensors, the wrist sensors have been used in multiple field studies with over 100 participants, and no significant skin irritation has been reported. Therefore, we assess the severity of the discomfort and irritation of wearing the wrist sensors to be minimal. If irritation persists to a point where the participant no longer wishes to participate, any irritation is entirely reversible once the participant removes the wrist sensors.

While electrical devices do introduce the risk of electric shocks, the probability of a participant experiencing even minor electrical shocks is negligible. High impedance circuitry is used to limit current flow, even in the case of external events (e.g., through physical breaking of the sensor board or shorting of the battery leads). All sensors in the wristbands are commonly used in mobile phones

and other activity monitors and pose minimal risk to participants. We expect that the wrist sensors, which have precedent of prior use in a research study or have otherwise been designed for everyday wear, will elicit similar acceptability among the participants in this study.

Regarding privacy concerns, participants' contact information will be linked to their study data via a code. The key to this code will be available only to the research staff at Dartmouth, and will be secured separately from the rest of the study data that is transmitted to the research team at the University of Memphis. Participants will be informed of their rights to terminate their participation in the study at any time. Participants will also be informed of their rights to remove the wrist sensors if they so choose, if they do not wish to be tracked. Moreover, participants will be informed of (and trained how to use) an interface on the smartphone that will suspend data collection. This feature is built into the software to allow participants the agency to suspend data collection and study-related engagement at their will, in the event that physically removing the wrist sensors would prove troublesome for the participant. Participants will be given a summary of the incentive structure, and will be informed how their participation will affect their final incentive payment.

All personnel that will be present for the research activities will be essential personnel in the conduct of this research. All personnel who will interact with participants at Dartmouth, and all personnel who interact with the participants' coded data at MD2K partnering sites, are trained in human participants research. Moreover, all study staff at the collaborative research sites external to Dartmouth will receive only coded data. No directly identifiable data will be provided to the collaborators, and the key linking participant codes to identifiers will not be shared under any circumstances. These collaborating personnel include Dr. Marsch and her study team at Dartmouth, Dr. Kumar and his study team at the University of Memphis, Dr. Ertin and his study team at Ohio State University, and Dr. al'Absi and his study team at the University of Minnesota. Only Dr. Marsch, Dr. Kumar, and their study teams will have access to the data; data will not be shared with Dr. Ertin, Dr. al'Absi, and their study teams.

Study participants will be informed that this research is conducted as part of a collaborative, multi-institutional research team. Study participants will be informed that coded data, which will not directly identify them, may be shared

among researchers at other institutions who are a part of the collaborative research team with appropriate IRB oversight.

Protection against risks from electronic databases: To protect the privacy or confidentiality of participants' data stored in electronic databases, every effort will be made to safeguard the confidentiality of research records, using data files free of information enabling individual identification of participants, lock-and-key access to paper records, and computer data files maintained with encryption, password protection, and behind firewalls. We will remove individual identifying information from data representations so that security failures would not put individual privacy and confidentiality at risk. Individual identifying information will only be maintained in a separate encrypted database with passwords known only to the PIs and specific members of the research team.

Each of the following sources of data is explained in detail separately: (1) eligibility, baseline, and follow-up; (2) EMA and Laddr (mobile intervention); and (3) mobile sensing (EMA-plus-mobile-sensing participants only).

(1) We plan for the eligibility, baseline, and follow-up assessment batteries and resulting data to be available and coordinated through Dartmouth's Research Electronic Data Capture (REDCap) system. All eligibility, baseline, and follow-up assessment data will be either acquired using REDCap forms or stored directly in REDCap upon acquisition. Participants will complete assessments via an encrypted Internet connection via 128-bit Secure Sockets Layer (SSL), the standard technology for securing eCommerce and eBanking transactions on the Internet.

(2) All EMA and Laddr usage data provided by participants when using the web-based Laddr® intervention will be stored locally on the phone in an AES-256 encrypted database. Data are stored in a key-value store residing on AES-256 encrypted SSDs (encrypted at-rest). Data are sent to the server when the device is online over an encrypted connection using SSL over HTTPS and will not be accessible to anyone not affiliated with the research project. The server is located in a locked cabinet, in card-key secured room, in a secure, monitored data center in Fremont, California. The server is behind multiple firewalls with intrusion detection systems in place. Security patches for system software are installed within days and

most often within hours after their release. All data stored on this server will be coded by participant ID number.

Dartmouth research staff will use an application, developed by the same team that developed Laddr, to initiate Laddr for participants. The team will download password-protected raw data files from a website created by the Laddr developers to monitor EMA completion and Laddr usage. These files will also allow the study team to track compensation amounts for each participant. Exported data will be identified via participant code and stored on password-protected computers.

(3) (EMA-plus-mobile-sensing participants only) Mobile sensing data will first be aggregated from the wearable sensors and the phones and will be stored in an encrypted format on the storage of the study-provided smartphones. In the event a phone is lost or stolen, the encryption will ensure that study data would be unreadable by anyone not on the study team. Aggregated wrist sensor data from the smartphone will be transmitted automatically to the computational cluster at the University of Memphis via the smartphones. All study data will be sent via a secure mobile data connection (HTTPS). At the conclusion of the study, the study manager will sync the smartphones with the computational cluster managed by the research staff at the University of Memphis to ensure all data collected by the smartphone platform have been recorded by the computational cluster. At the computational cluster, University of Memphis research staff will ensure the quality of the data received from the smartphones and will manage the export routines for approved users (investigators and staff) to access the data.

The computational cluster is electronically firewalled, encrypted, password-protected, and physically secured. Data are secured on the cluster using (1) a firewall that limits access to a whitelisted set of IPs/subnets, (2) 2048-bit SSH keys for authentication of individual access accounts, and (3) VPN access for those computers/individuals that do not fit into the set of whitelisted IP addresses. Data security will be provided by limited-access accounts in which each individual will explicitly be granted access only to the datasets for which they are authorized. Dartmouth research staff will have the means to log into the export interface with the computational cluster to allow for monitoring of participant adherence to the study protocol (e.g., to monitor that

participants are wearing the sensors). Dartmouth research staff will also use this interface to export wrist sensor data streams for analyses. Exported data will be identified via participant code and stored on password-protected computers.

After completion of the study, a de-identified dataset (i.e., stripped of all codes or other information that could be linked back to an individual participant) will be generated and made available to the research community as a whole. Informed consent procedures will ensure that participants are aware that consenting to participate in the study means consenting to inclusion in this open data set.

All information that is collected from the participants will be the minimum necessary, and de-identified to the maximum extent possible, to conduct the research. Study participants will be informed that research data collected about them will be stored at Dartmouth (and for EMA-plus-mobile-sensing participants, the University of Memphis) until they are no longer useful. It is estimated that the data will possibly be useful for 10 years, but the data may be useful and may continue to be retained indefinitely. Eligibility data from the screening questionnaires will be retained for those who participate but will be deleted at the end of study for those who screen out or choose not to participate. Data may be retained indefinitely for those who screen in and sign consent but do not become part of the analytic sample due to technical difficulties or low participation.

Potential Benefits of the Proposed Research to Human Subjects and Others

As Aim 2 is not a clinical or therapeutic study, there are few direct benefits of the proposed research to the participants; however, the information to be gained from their participation may benefit others in the future. Additionally, participants may learn self-regulation techniques through the Laddr mobile application.

Importance of the Knowledge to be Gained

The proposed activities are designed to identify valid and replicable assays of mechanisms of self-regulation across populations to inform an ontology of self-regulation that can ultimately inform the development/refinement of health behavior interventions of maximal efficacy and potency. Because the need to alter health-related behavior is ubiquitous across medicine, understanding the

extent to which the principles of effective health behavior change, and the mechanisms by which they work, are similar or different across health conditions and settings is a critically important area of scientific inquiry. It may inform more efficient, cost-effective, and patient-centered care. This line of research may ultimately allow us to make great strides in crafting "precision medicine" approaches for a wide array of populations. Given the importance of the knowledge to be gained, the risks to the participants are reasonable, as the risks are minimal and plans for protection against these risks are in place.

Data and Safety Monitoring Plan

Consistent with best practices, the Principal Investigator (Dr. Marsch) will oversee all data and safety monitoring functions (described above) to ensure the safety of participants in the proposed study and to ensure the validity and integrity of the data obtained in the study. The Principal Investigator will also regularly meet with the Project Manager, Research Assistants, and Co-Investigators to track study progress and review these monitoring procedures. The Principal Investigator will regularly oversee all aspects of the study, including participant recruitment, informed consent, data collection, data management, and data analysis procedures, as well as regularly assess the risk/benefit ratio associated with participation in the study**.**

The Principal Investigator will train all project staff to recognize and report any adverse event immediately to them. Adverse events involving human participants include, for example, physical injuries, worsened physical or mental health, suicidal ideation, panic attacks, and depression. Other adverse events may also include the inadvertent disclosure by research staff of confidential research information to other persons and/or to staff of criminal justice or government agencies.

In the event that such adverse events are reported to the Principal Investigator, she will immediately inform the Chairperson of the appropriate Institutional Review Board, who will make a decision about whether the reported event is a Serious Adverse Event (SAE) that must be reported to the appropriate Federal Agency. If the Principal Investigator determines that there is sufficient evidence of an adverse event to necessitate suspension of data collection, further IRB review, modification of the protocol, or other changes, the Principal Investigator will immediately discuss this recommendation with the Chairperson of the IRB and

reach a determination of whether to suspend data collection or to stop the study from proceeding. Resumption shall be based on the concurrence of the Principal Investigator, the Chairperson of the IRB, and any other relevant parties. The Federal Agency will receive a written report within three days of any such suspension and/or resumption of data collection.

The Principal Investigator will provide an annual summary report of all adverse events to the IRB as part of the annual review and to the Federal Agency as part of the annual Progress Report. If no adverse events have occurred, the report will state, "No adverse events affecting human participants have occurred during this project year."

Protocol Updates

December 20, 2017

- Eligibility criteria
    - Both groups:
        - Removed the depression exclusion criteria. We will measure it and potentially use it as a covariate.
    - Smoking:
        - Reduced smoking requirement to ≥ 5 tobacco cigarettes/day (was ≥ 10/day)
        - Reduced maximum BMI to < 27 kg/m^2 (was < 30 kg/m^2)
    - Binge eating:
        - Reduced minimum BMI to ≥ 27 kg/m^2 (was ≥ 30 kg/m^2)

February 9, 2018

- Expanded recruitment from continental United States to entire U.S., including U.S. districts and territories.
- The study team will no longer use Labs to initiate and monitor Laddr usage. (Laddr is the self-regulation mobile application used by participants.) Instead, the study team will use an application, developed by the same team that developed Laddr, to initiate Laddr for participants. The team will download password-protected raw data files from a website created by the Laddr developers to monitor EMA completion and Laddr usage. These files will also allow the study team to track compensation amounts for each participant. Exported data will be identified via participant code and stored on password-protected computers.
- Increased the sample sizes such that the EMA-only sample size will be up to 100 participants (50 in the smoking group and 50 in the binge eating group; same as before), and the EMA-plus-mobile-sensing sample size will be up to 50 additional participants (rather than up to 50 of the originally proposed 100 participants). The proposed sample sizes consist of participants who initiate usage of Laddr, the behavior change mobile application; there may be a greater number of participants who sign consent but do not participate beyond the baseline questionnaires.

March 7, 2018

- Increased sample sizes to reflect the number of participants who sign consent but participate minimally and are excluded from the analytic samples. Included plan to retain all data from these participants.
- Specified electronic compensation method as Amazon gift card; specified details necessary for sending a check. Added more detail to the compensation schedules.
- Removed mobile sensing requirement from bonus in EMA-plus-mobile-sensing samples.

March 19, 2018

- Updated consent forms for the EMA-plus-mobile-sensing smoking sample and both the EMA-only and EMA-plus-mobile-sensing binge eating samples. (Consent for EMA-only smoking sample is not updated because recruitment and data collection for that sample are complete.) The additional optional consent at the end of the document regarding inclusion in a de-identified, publicly available dataset has been moved into the consent for participation. All participants must agree to be included in the publicly available dataset in order to participate in the study. Corresponding language has been updated in the Protection of Human Participants section above to reflect this revision. This change is being made to better align with NIH guidelines, including those specific to the Science of Behavior Change initiative.
- Additional minor edits:
    - Changed Aim 4 objective measure for binge eating sample to exercise because of lack of objective eating measures.
    - Expanded on name of I-7 baseline measure for further clarity.

May 7, 2018

- Updated protocol and EMA-plus-mobile-sensing consent forms to include possibility that study staff may request government-issued photo identification to verify the age and identity of the EMA-plus-mobile-sensing participants.
- Updated some language from “mobile sensing” to “EMA-plus-mobile-sensing” to enhance clarity that the participants engaged in mobile sensing also complete EMAs like the EMA-only participants.

- Updated all mentions of “obese” to “overweight/obese” given the BMI range of 27 to 45 (inclusive).