Internet Assisted Obesity Treatment Enhanced with Financial Incentives

NCT02688621

Document Date: February 6, 2015

The University of Vermont Committees on Human Research

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PROTOCOL NUMBER

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PROTOCOL SUMMARY

Project Title:	Protocol Version Date:
Internet Assisted Obesity Treatment Enhanced with Financial Incentives	1/26/2015

Principal Investigator: Jean Harvey

Grant Sponsor: NIDDK Grant Number: RO1 DK056746

(For grants routed through UVM, indicate the OSP Proposal ID # located at the top of the OSP Routing Form)

Lay Language Summary: *(Please use non-technical language that would be understood by nonscientific IRB members to summarize the proposed research project. The information must include: (1) a brief statement of the problem and related theory supporting the intent of the study, and (2) a brief but specific description of the procedure(s) involving the human subjects. Please do not exceed one single-spaced 8 ½ X 11" page.)*

Obesity is an epidemic in the United States, and it is extremely costly to care for those with obesity-related illnesses. Behavioral lifestyle interventions have been shown to successfully produce clinically significant weight

losses and improve health. Internet-delivered weight control programs have been shown effective in producing clinically-significant weight losses, with the approach to web-based obesity treatment our research group has developed producing some of the largest weight losses reported in the literature to date. However, weight losses remain modest with online delivery, undercutting the potential impact of technology-enhanced delivery. ***Therefore, the overall goal of this project is to continue the work of our group in identifying strategies to enhance weight loss outcomes produced by an online-delivered behavioral program by examining the promising strategy of providing financial incentives within the context of treatment***. We propose a randomized, controlled trial to determine whether incorporating financial incentives increases the amount and duration of weight losses achieved by Internet-delivered behavioral treatment. A secondary, exploratory aim is to quantify the incremental cost-effectiveness of each intervention strategy compared to established cost-efficacy thresholds. Overweight and obese adults at two study sites (UVM and University of South Carolina [USC]; N=416; 27% minority) will randomized to: (1) Internet intervention; or 2) Internet intervention plus financial incentives for implementation of key self-management behaviors (daily self-weighing, self-monitoring of dietary intake and achieving step goals) (Internet+Incentives). All participants will receive the same 36-session web-based group weight control program which features synchronous, facilitated chats and online behavioral tools. Assessments will be conducted at 2, 6, 12- and 18 months and will include measures of body weight, treatment engagement (e.g., attendance, self-monitoring, website utilization, motivational factors, weight control behaviors) and treatment delivery cost.

PURPOSE AND OBJECTIVES

Purpose: *The importance of the research and the potential knowledge to be gained should be explained in detail. Give background information.*

Obesity is an epidemic in the United States.[1] The majority of the population is overweight or obese, and the cost of caring for those with obesity-related illnesses is expected to rise to 861-957 billion dollars by 2030.[2] Fortunately, weight losses of as little as 5-7% of body weight can ameliorate many of the co-morbidities associated with obesity.[3] Behaviorally-based lifestyle interventions have been shown to successfully produce these clinically significant weight losses;[4,5] however, the reach and availability of existing lifestyle programs is limited. The Internet as a medium for delivering health behavior interventions has received increased attention, particularly for weight loss and maintenance.[6-12] In fact, our research group has achieved some of the most significant weight loss results to date in Internet-based programs, with clinically significant weight loss in over half of those participating.[13] Unfortunately, these weight loss results, and those of others delivering web-based programs,[9] are not yet as substantial as those achieved with in-person programs. Despite this limitation, technological solutions to obesity have only increased in popularity and have proliferated. **Therefore, the overall goal of this project is to advance public health interests by identifying strategies to enhance weight loss outcomes delivered online, specifically through the use of economic incentives**.

Sixty-nine percent of adults in the US are considered overweight, and 35% meet the criteria for obesity.[1] The aggregate direct medical costs associated with obesity in the US are estimated to be 114 billion dollars annually,[22] and obesity is significantly associated with an increase in mortality.[23] Thus, it is no

surprise that obesity is a key public health concern for the century ahead. Although effective obesity interventions have been developed,[24,25] access to these interventions is limited in many areas of the country.

One of the strengths of Internet-based behavioral obesity treatment programs is the ability to reach individuals who might not otherwise have access to weight loss programs. However, Internet-based interventions have not yet achieved the same degree of weight loss as in-person interventions,[13] although our research group has achieved some of the largest weight loss results (-5.7%) to date in Internet-based programs, as well as clinically-significant weight loss in over half of those randomized to an online weight loss program.[13] Despite modest outcomes, the popularity and promise of Internet and other technology-mediated delivery of weight management can be seen in the proliferation of offerings by commercial weight loss programs (e.g., Weight Watchers), the popularity of weight management apps like My Fitness Pal and Lose It!, and the increase in technology-based programs in worksites.[8,26-34] ***Therefore, it is important to identify strategies that can enhance weight loss outcomes in online programs so that policy makers and program developers can incorporate effective elements into future weight loss initiatives.***

One strategy that holds promise for increasing engagement and enhancing outcomes is financial incentives. The neo-classical economic framework suggests that the optimal decision for some (perhaps most) individuals may be to engage in a lifestyle that leads to excess weight. In other words, well-intentioned, rational, utility-maximizing individuals may believe it is just too costly (in economic terms) to weigh less, and they therefore knowingly choose a lifestyle that leads to excess weight. Economic incentives have the potential to alter that outcome by increasing the benefits of weight loss (it now generates additional income). Contingency management theory (CM)[35] would also support the power of incentives to modify behavior by altering the consequences. Incentives provide positive feedback and reinforcement for successfully meeting goals and may therefore help sustain behaviors that led to successful weight loss, irrespective of their financial value.

Early research demonstrated that incentives may be effective in promoting weight loss,[18-20] although important questions remain about best practices for achieving sustained weight loss with incentives. Initial investigations coupled incentives with interventionist contact in the context of a structured behavioral program,[36-39] but recent research has coupled incentives with short-duration interventions[18-20] that included weigh-ins only, health education materials or minimal therapist contact[18-20,40-42] Longer-term effects have been modest,[43] perhaps because the incentives seldom were incorporated into an effective, evidence-supported behavioral intervention such as proposed in this application. *The current study will evaluate the impact of incentives in the context of a robust and replicable online behavioral intervention with regular therapist contact and an extended18-month intervention to advance our understanding of the full potential of economic incentives in weight management.*

Most previous work that incentivized weight loss has targeted weight loss outcomes rather than the behaviors necessary to achieve them, which may underestimate the full potential of incentives in promoting weight loss.[43-45] Further, little of the available research on incentives in weight control has focused on weight maintenance,[46] and available studies showed no significant improvement using

incentives in weight maintenance.[43,47,48] We have elected to incentivize key self-management behaviors, specifically daily self-weighing, dietary intake self-monitoring, and increased physical activity. These behaviors are associated with greater weight loss in both in-person treatment[49-54] and online programs.[6,8,9,55] Preliminary work by Dr. Leahey, consultant on this project, demonstrates that the addition of incentives contingent upon this suite of behavioral targets can produce a 2.2 kg increase in weight loss in combination with a minimal online treatment program, compared with the same program without incentives. Similarly, Dr. Finkelstein, consultant on the study, found incentives increased physical activity in the short term.[56] *Thus, selecting behaviors strongly associated with successful long-term weight control as incentive targets offers significant promise for promoting weight loss.*

The most effective incentive strategy to promote weight management behaviors is unknown. Some[19,57] hypothesize that an approach that offers frequent chances to win small payouts based on meeting short-term goals and less frequent chances to win larger payouts based on longer-term goals will be more effective than a straight pay-for-performance approach (of equal expected value). Noting the CM literature, they contend that frequent small payoffs provide positive and timely reinforcement and the large payoff provides additional benefit because of evidence that people are emotionally attracted to small probabilities of large rewards and overestimate their chances of "winning" a large payoff. As a result, the small chance at a high payoff may provide greater motivation than the smaller certain payout. Volpp et al.[19] further argue that an incentive strategy that puts an individual in a position of losing a given amount of money if weight loss is not achieved will be more effective than an incentive in which an individual is paid for meeting the goals, based on the psychological concept of 'loss aversion.'[58]

Some have suggested that transitioning from a fixed schedule of incentives, which can support initial change efforts, to a variable incentive structure during the maintenance phase may reduce habituation to the incentives and buffer against extinction.[44,46] The confluence of incentivizing behaviors and transitioning from a fixed reinforcement schedule to a variable schedule may offer maximal opportunities for increased and durable weight loss outcomes. An online treatment milieu allows for delivery of incentives in real time with minimal delay between behavior and reinforcement. The immediacy of reinforcement would be expected to enhance the potency of incentivizing weight-loss-related behaviors, based on learning theory and behavioral economic research.[59,60] ***Incentives added to an online obesity program provide an opportunity to maximize technology for both broad delivery of obesity treatment and promoting weight control***.

Another appeal of Internet-delivered obesity treatment is that it may be more cost-effective than the same program delivered in-person. Our previous work has demonstrated this.[61] The reduction in treatment barriers that online delivery can offer is also very attractive. Methods to increase the magnitude of weight loss that can make online delivery cost-effective from the perspective of the treatment delivery agent are needed. The addition of incentives to an intensive program like ours could increase the short- and long-term weight losses achieved and potentially be cost effective for the payer.[62] ***Few studies of incentives in weight loss have included a cost effectiveness component, but the time is right to examine this important dimension.***[63]

Therefore, the current application proposes to examine incentives within the context of our online weight management program, which features synchronous facilitated chats and online behavioral tools and which has achieved impressive average weight losses of 6.0% in two separate trials. We propose to

compare this Internet program with the same online program augmented by financial incentives for behavioral engagement.

***References**. Include references to prior human or animal research and references that are relevant to the design and conduct of the study.*

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Objectives: *Clearly state the primary and secondary objective(s) of the study.*

Aim 1: To test whether incorporating incentives can increase the amount and duration of weight loss achieved by Internet-delivered behavioral treatment.

Aim 2: To quantify the incremental cost-effectiveness, in terms of costs per quality adjusted life year saved, of the incentive-based program compared to the Internet-delivered program without incentives.

METHODS AND PROCEDURES

Study Design: *Describe the research design, including a description of any new methodology and its advantage over existing methodologies.*

Overview. We propose a randomized controlled trial to evaluate whether the addition of financial incentives to a high-quality, online behavioral weight loss intervention produces better weight losses than the online treatment alone. Overweight and obese but otherwise healthy participants (N=416) will be randomized to one of two conditions: 1) an 18-month, 36-session group Internet behavioral weight control treatment (Internet) which replicates the intervention we have implemented previously; or 2) the same 36-session group Internet treatment plus financial incentives for performance of 3 key self-management behaviors (Internet+ Incentive). Both conditions will have access to the same web-based intervention platform and the same counselor-delivered intervention elements; the presence of economic incentives for behavioral and weight goals is the only difference between the conditions. Assessments will be conducted at 0, 2, 6, 12 and 18 months.

Internet Behavioral Weight Control Treatment. We have developed and implemented a theory-based group-delivered online behavioral weight control program in two previous studies that incorporates the elements of current thinking and empirical data on successful weight loss programs,[24,53,72] including restricted calorie intake and increased physical activity. Key behavioral strategies to facilitate making sustained changes in dietary habits and activity patterns are introduced, promoted and reinforced throughout the program. Synchronous chat (i.e., in real time) sessions facilitated by an interventionist provide the "group meetings," and extensive web-based resources support behavior changes. The program provides 24 weekly facilitated group chats over the first 6 months followed by 12 monthly chats, for a total of 36 "group sessions." Target weight losses of 10% of baseline weight are promoted. Behavioral strategies are drawn from social cognitive theory[73] and self-regulation theory[74] and mirror the core components incorporated into such successful programs as Look AHEAD.[25] *Importantly, we propose to include the same dietary and physical activity prescriptions, identical behavioral strategies to reach these goals, and the same delivery format and number of sessions in both treatment arms; thus the content of the two conditions will be comparable, allowing only the presence of incentives to vary between the conditions.*

Financial Incentive Structure for Internet+ Incentive Condition. We propose to incentivize behaviors that are consistently and robustly associated with successful weight loss, and also theoretically important from a self-regulation perspective.[74] Specifically, we propose to reinforce or incentivize three behaviors: self-weighing and reporting of body weight; self-monitoring of dietary intake, and increased physical activity (achieving step goals). Self-weighing has emerged as an important behavioral strategy in weight management;[52,75-77] as noted above, our iREACH data indicate that the practice is predictive of weight loss at 1 year, and our work in Look AHEAD demonstrated that the individuals who were the most successful at 8 years were more likely to weigh themselves daily.[54] Our iREACH data suggest that online recorded weights are quite accurate,[78] and our proposal to incentivize reporting body weight rather than the actual weight observed will help reduce "gaming" or inaccurate reporting. In a randomized trial, a minimal behavioral intervention that focused on daily self-weighing produced better weight losses than the same intervention plus a scale but no directions to weigh daily.[79] Similarly, self-monitoring of dietary intake has been repeatedly demonstrated to predict better weight losses[4,49,80] and is a central self-management strategy to provide important objective feedback, even if it

may not be fully accurate.[81,82] Increased physical activity is another strong predictor of successful long term weight control,[54,83] and we have elected to focus on increasing the number of steps taken, as walking is the exercise in which our participants are most likely to engage. We propose to incentivize achieving a step goal (with methods to get "credit" for swimming or cycling) that incrementally increases the step count required for the incentive payout; this approach will nudge along physical activity increases tailored to an individual's baseline step status. Goals will call for an initial increase of 2000 steps per day over baseline[84,85] (which will be increased by another 2000 steps every 4 weeks). This use of tailored step goals which gradually increase over time will allow us to incentivize increased physical activity even among those who are already active in their occupational pursuits, as well as for those for whom a 10,000 step goal at the initiation of treatment would present risks of injury. Further, this approach to incremental increases in step goals is associated with enhanced fitness, another correlate of successful weight loss [86] and an important outcome in and of itself.[87] We will identify physical activity apps for participants to allow steps to be objectively tracked and to provide the basis for obtaining incentives for this behavior.

Table 1. Incentive Strategy

Randomly Selected Payout Day		Incentive Payout
Weighed Self and Reported Weight (yes/no)	On 3 previous days	$3
	On 2 previous days	$2
	Yesterday only	$1
	Not yesterday	$0
Self-Monitored Dietary Intake (yes/no)	On 3 previous days	$3
	On 2 previous days	$2
	Yesterday only	$1
	Not yesterday	$0
Met Tailored Step Goal	On 3 previous days	$3
	On 2 previous days	$2
	Yesterday only	$1
	Not yesterday	$0

Incentive Schedule. The incentive schedule we propose will provide an incrementally graded payout for sustained performance of these key self-regulation behaviors. Specifically, we seek to provide greater incentives for those who have engaged in the behaviors over the course of several days (see Table 1). For participants in the Internet+Incentive condition, once a week a "payout" day will be randomly selected from the previous week. Participants who engaged in the target self-management behaviors (weighed self and reported weight, self-monitored dietary intake, and/or achieved their tailored step goal) on that randomly selected "payout day" will receive a modest incentive ($1) for each of the three independent behaviors. If the participant engaged in the behavior on the day before the payout day, then the incentive will be doubled ($2) and if the participant engaged in the behavior on both the previous days (for a total of three days in a row), the largest payout will be received ($3). Thus, a participant who performs all three behaviors consistently has the opportunity to earn $3 for each of 3 behaviors (for a total of $9 each week) during the first 6 months of the program. Individuals who did not engage in the behavior on the randomly-selected payout day will receive no incentive. Small incentives have been shown to be effective in promoting behaviors and weight loss.[18-20] Each participant will be notified by email or text (their preference) of the incentive received for each behavior and the total amount received that week. The message will highlight the incentive they received (reward message) AND the incentive they *could* have received (a loss message) to incorporate regret aversion, which may well be more powerful a motivator of behavior change than reward *per se.*[88] We propose to also use loss aversion message framing in reminders sent to participants about upcoming opportunities for incentives (e.g., don't miss out on your money, be sure to submit….). Incentives will be automatically posted to an Amazon.com account to allow the participant access to the funds in a proximal fashion, offering immediate access and thus greater salience of the reward.

We propose to payout half of the incentive participants have earned immediately (at the time they get the message of their incentive amount). This provides the proximal reinforcement that the contingency management perspective indicates will be most powerful. We propose to place the other half of the

incentive earned during the week in an “incentive savings account,” which will accrue in value as weekly incentive ”deposits” accumulate. The participant will have access to recouping these accrued incentive payouts by achieving modest weight loss goals at 2, 6, 12 and 18 months, and they will have further opportunities to double their savings amount if they have achieved substantive weight loss goals. Those who fail to achieve the modest weight loss goals will forfeit their savings account from that period. This incentive strategy allows us to institute a paradigm that heightens loss aversion but also provides an incentive to increase weight loss to further increase financial gains. Thus, the more participants do to earn the short-term rewards, the more they stand to lose by not reaching the next weight loss goal and the more they stand to gain by exceeding those goals. This theory-based approach has a high chance of generating both greater weight loss and greater weight loss maintenance. The intervention website will maintain a current balance of each participant’s incentive savings account and a reminder of when the savings payout will be. A calculator which allows the participant to project into the future what the payout would be if he or she were to engage in the targeted self-management behaviors will also be available. This will both allow us to emphasize the strong connection between engaging in the self-management behaviors and building the incentive amount, as well as to accentuate the potential incentive amounts available with substantive weight loss (and that could be sacrificed without goal attainment).

Possible Incentive Which Can be Earned in Each Period

Study Month	Intervention Contact	Incentive Schedule	Payouts
Months 1 to 2	**Weekly** chat sessions (Total = 8)	At end of week, one day from previous week randomly selected Total= 8 payouts	Maximum Payout = $72 (8 * $9) ½ available immediately (up to $36) and ½ put into Savings
Upon weight verification at 2-month Data Collection Lost <3% Forfeit Incentive Savings Account Lost ≥3% Get payout of full Incentive Savings Account — Max Payout = $36 savings Lost ≥5% Payout doubles amount in Incentive Savings Account — Max Payout = $72 (double savings)			
Months 3 to 6	**Weekly** Chat Sessions (total = 16 sessions)	At end of week, one day from previous week randomly selected Total= 16 payouts	Max Payout = $144 (16 * $9) ½ available immediately (up to $72) and ½ put into Savings
Upon weight verification at 6-month Data Collection Lost <5% Forfeit Incentive Savings Account Lost ≥5% Get payout of full Incentive Savings Account — Max Payout = $72 savings Lost ≥10% Payout doubles amount in Incentive Savings Account — Max Payout = $144 (double savings)			
Months 7 to 12	**Monthly** Chat Sessions (total = 6 sessions)	Randomly select pay day on 16 occasions Total= 16 payouts	Maximum Payout = $144 (16 * $9) ½ available immediately (up to $72) and ½ put into Savings
Upon weight verification at 12-month Data Collection Lost <5% Forfeit Incentive Savings Account Lost ≥5% Payout of full Incentive Savings Account + $25 bonus — Max Payout = $72 savings + $25 bonus = $97 total payout Lost ≥10% Payout doubles Incentive Savings + $50 bonus — Max Payout = $144 double savings+ $50 bonus = $194 total payout			
Months 13 to 18	Monthly Chat Sessions (total = 6 sessions)	No Incentive	

As outlined in Table 2, over the course of the initial 2-months, participants will have the opportunity to earn $72 for engaging in the three self-management behaviors. They will have immediate access to half of the incentive value earned (a possible total of $36) in eight weekly installments and the remainder will go into their "incentive savings account," which affords them the opportunity to double the amount in the savings account if they achieve weight loss goals in addition to behavioral goals. At 2 months, if they have achieved at least a 3% weight loss, they will get a payout from their savings account (a total possible of $36). This ≥3% incentive payout threshold derives from our Look AHEAD data which indicate that those who achieve this magnitude of weight loss at 2 months go on to lose an average of 10.75% at 1 year.[68] As an added inducement to achieve early success, we will double their incentive savings account (for a payout of up to $72) if they have achieved ≥5% weight loss by 2 months. Our Look AHEAD data indicate that individuals who have lost ≥5% at 2-months achieve a 12.72% weight loss at 1 year and that 64% of these individuals will have lost at least 10% by 1 year. Participants who have failed to achieve at least the 3% weight loss will forfeit their savings account. By incentivizing these thresholds, we hope to swell the proportion of participants who achieve early weight loss milestones which appear to lead to later weight loss milestones. Messages which accompany the payouts will be framed to reinforce loss, when appropriate, and emphasize opportunities for the next payout period so as to allow re-engagement while also heightening potential loss aversion.

A similar approach to winning back the "incentive savings account" by achieving target weight loss goals will be used at the remaining data collection points. At 6 months, individuals who have achieved the 5% weight loss goal will be rewarded with their accumulated incentive savings account (a maximum of $72 in savings, with another $72 that would have been paid out in weekly installments over 16 weeks). Those who have lost ≥10% will be eligible for a payout of up to $144 (or double their savings amount) after the 6-month assessment. Those who fail to reach the 5% threshold at 6-months will forfeit their incentive savings to date (but not future incentive savings).

As we transition into monthly chat sessions (at 6 months), and begin to focus on weight maintenance skills, we propose to transition to a variable reinforcement schedule. Further, we propose to reduce the frequency of payouts so that we are implementing a less dense reinforcement schedule. In the absence of research which defines the best incentive structure to promote weight loss maintenance,[46] we selected a strategy which gradually moves to a less frequent and also less predictable schedule, which would be likely to offer greater likelihood of sustainability (or resistance to extinction). From 7-9 months, 3 payout days will be randomly selected in 3 out of 4 weeks each month (and participants will not be informed of this schedule, but be told that payout days are now totally at random). Incentives will still be awarded incrementally based on the number of consecutive days performing the three behaviors. A total of $9 is available at each payout day, and half of the incentive earned during this phase will be placed in the "incentive savings account." We will again transition to a less dense reinforcement schedule at the 10-12 month period, reducing the number of weeks with a payout to 4. Individuals who have at least a 5% weight loss at 12-month data collection will get their savings account along with a $25 bonus for their weight loss. Those participants who have a 10% weight loss at 12 months will get their incentive balance doubled plus a $50 bonus for their weight loss. Those who have not lost 5% will not get any incentive. The addition of a bonus payment for weight loss is designed to allow some payout to participants who have achieved the target weight loss but who have elected to stop engaging in the self-management behaviors (or to stop reporting the behaviors to us). Although we are concerned that discontinuation of these critical self-management behaviors may render an individual vulnerable to relapse and weight regain,[89,90] we also recognize that achieving the weight loss targets is the ultimate goal and we therefore have adjusted the incentive strategy to incorporate this.

The final six months of the program (months 12 to 18) will examine the durability of the self-management habits and weight loss trajectory in the absence of financial incentive. This will expand our understanding of whether weight control supported by incentives will continue in light of the possible discontinuation of incentives. Comparison of weight losses at 18 months between the Internet and Internet+Incentive conditions will allow us to determine whether weight loss outcomes among those with a history of incentives to motivate weight control (which are no longer present to enhance motivation) differ from the outcomes of individuals who never experienced incentives to promote weight loss.

Measures. The following measures will be taken at 0, 2, 6, 12 and 18 months unless otherwise noted. Questionnaires will be computer administered to facilitate data management and capitalize on online accessibility of all participants, although paper versions will be available if needed. Weight outcomes will be obtained in person.

Weight and Adiposity. **Change in body weight is the primary study outcome.** Weights will be taken in street clothes without shoes using a calibrated hospital-quality digital floor model scale. Height will be taken at baseline using a wall-mounted stadiometer. Weight change will be calculated as kg lost from baseline and % of baseline body weight lost. BMI will be calculated as weight (kg)/height (m^2). We will also examine the proportion of individuals who achieve clinically significant weight losses of $\geq$5% and $\geq$10%.

Sociodemographic Characteristics. Participants will complete a sociodemographic questionnaire at baseline that includes locator information (i.e., friends or family who will have current contact information) for assistance in tracking individuals who move or are difficult to contact.

Process Measures**.** We propose to capture important dimensions of treatment engagement to allow examination of adherence overall, as well as potential mediators of weight loss outcomes.

Intervention Participation. We will record attendance at chats, self-monitoring rates for body weight, dietary intake and physical activity, as well as website utilization, to get a sense of intervention participation levels across the two conditions. Our work and that of others indicates that attendance and self- monitoring are both robust predictors of weight loss outcomes,[6,8,9,49-51,53,55,91] and we have also shown that website log-in frequency appears to be related to weight loss success.[91] The current study will shed light on the role of incentives in promoting participation in treatment and whether increased participation mediates any increases in weight loss observed.

Dietary Intake. Participants will complete the Automated Self-Administered 24-hour recall (ASA24) to assess usual dietary intake, using an online program developed by the National Cancer Institute.[92] Nutrient variables examined will include total calories and percent of calories from fat, which will allow us to characterize the groups and interpret energy intake differences that might illuminate weight loss differences.

Physical Activity. The Paffenbarger Physical Activity Questionnaire (PPAQ)[93] is a standardized questionnaire that assesses leisure time activity, including stairs climbed, distance walked and other leisure time activities. Thus, it assesses physical activity behaviors emphasized during the treatment program. Although the PPAQ is subject to self-report bias and provides only a modest correspondence with fitness,[94] it is economical, has low participant burden and has been shown to distinguish behavioral treatment conditions in previous studies.[95] Inclusion of this measure will allow a standardized

assessment and comparisons between conditions on an important parameter that we are incentivizing in one condition. We considered a more objective measure of physical activity but elected not to include this because of cost considerations and because physical activity is not a primary outcome.

*Motivation***.** Questions have been raised about the impact of incentives on autonomous motivation to change;[44,96,97] will individuals who change behavior in response to incentives attribute their change to external factors controlled by others? We have demonstrated that increases in controlled motivation are associated with poorer weight loss outcomes over the short-term, while increases in autonomous motivation are associated with better weight loss outcomes.[98] By examining how incentives impact motivational factors, this study can contribute important insights. We will assess motivation for participating in a weight control program using the 15-item Treatment Self-Regulation Questionnaire (TSRQ),[99] a self-determination theory-based measure which assesses autonomous reasons for engaging in weight control efforts (personal reasons for change or motivation that reflects a self-selected rationale for change) and controlled motivation (reasons for change that are imposed externally or emanating from others), a measure we and others have used previously to examine obesity treatment outcomes.[99-101]

Weight Control Behaviors Checklist. This self-report inventory of behaviors that have been associated with effective weight management was developed for the Look AHEAD trial and has been demonstrated in our work to predict who is likely to lose weight and keep it off for extended periods.[54] Daily weighing was associated with greater likelihood of sustained weight loss of ≥10% at 8-years and therefore is one of the linchpin behaviors in our proposed the incentive strategy.

Economic Measures. We propose to carefully monitor all costs for treatment delivery and incentive payouts. In addition, participants will complete the Euroqual 5D (EQ-5D), a health-related quality of life measure which can be used to examine Quality Adjusted Life Years (QALYs). This self-administered 5-item questionnaire indexes five dimensions of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and has been used in broad range of populations to provide quality of life estimates.[102,103]

Procedures: *Describe all procedures (sequentially) to which human participants will be subjected. Identify all procedures that are considered experimental and/or procedures performed exclusively for research purposes. Describe the types, frequency and duration of tests, study visits, interviews, questionnaires, etc. Include required screening procedures performed before enrollment and while on study. Please provide in table, list or outline format for ease of review. (describe and attach all instruments)*

Note: A clinical research protocol may involve interventions that are strictly experimental or it may involve some aspect of research (e.g., randomization among standard treatments for collection and analysis of routine clinical data for research purposes). It is important for this section to distinguish between interventions that are experimental and/or carried out for research purposes versus those procedures that are considered standard therapy. In addition, routine procedures performed solely for research purposes (e.g., additional diagnostic/follow-up tests) should be identified.

Individuals interested in participating will be directed to a secure online recruitment

webpage which queries for basic contact information and eligibly criteria (self-reported height and weight, age, etc.) and provides additional information regarding the study. Individuals who appear likely to be eligible based on this online registration will receive a brief phone screen conducted by research staff to confirm initial eligibility for the study and will be scheduled for an in-person orientation session where the study will be reviewed in detail, questions will be addressed and an informed consent

document will be provided to take home. After considering the study for a minimum of one week, participants interested in enrolling in the study will be asked to sign a consent form approved by the local institution (UVM or University of South Carolina) and baseline data collection will begin, including collection of height and body weight data. Participants will be asked to record dietary intake for one week as a behavioral run in and to complete questionnaires online. Directions for how to access both these elements will be provided to participants and a helpline contact will be provided. To be fully eligible, participants must also log in at an appointed time to "practice" chatting as a final run to assure they are able to access the web-based program and engage in it. Only after all these eligibly criteria have been satisfied will participants be randomized.

The College of Medicine Bioinformatics Facility Interactive Voice Response (IVR) system will be used to randomize groups of individuals to treatment condition. Dr. Ashikaga will access the IVR system and will use distributional characteristics of the baseline BMI of the intact groups to randomize to achieve between treatment arm balance. The current iREACH study has utilized the 25th, 50th and 75th percentiles of each intact group and has been successful in allocating groups to treatment conditions with little variation between groups compared to within group variation.

The group-based online behavioral weight control program incorporates the elements of current thinking and empirical data on successful weight loss programs,[12-14] including restricted calorie intake and increased physical activity. Key behavioral strategies to facilitate making sustained changes in dietary habits and activity patterns are introduced, promoted and reinforced throughout the program. Weekly "group meetings" in a synchronous chat (i.e., in real time) led by the interventionist are the venue for the group process and extensive web-based resources to support behavior changes are offered. The online groups are "closed" such that those individuals who start the group remain in that group for the duration of their participation. Group chat sessions meet weekly for 6 months (24 sessions) and then monthly for 12 months (total of 36 sessions over 18 months). ***Participants in both study conditions will receive this weight control program.***

Behavioral Weight Control Program Treatment Components: the iREACH program

Diet. While the primary emphasis of the dietary intervention is to restrict calories and stay below the prescribed goal, participants are also encouraged to eat a diet in line with the current U.S. Dietary Guidelines and the Food Guide Pyramid. Participants are asked to target fat intake in addition to overall caloric intake because data from a number of studies suggest that when fat and calories are both controlled, weight loss is superior. Therefore, participants will be given a fat gram goal which is 25% of their calorie goal. For example, someone with a calorie goal of 1400 kcal/day would have a fat gram goal of 38 grams/day.

Participants will record their calorie and fat intake daily. They will have access on the study website to calorie and fat gram guides which use pull down menus and personally customized calorie/fat counters to facilitate ease of recording. Participants are instructed to record (electronically) all food they consume and the calories and fat grams in those foods. The self-monitoring diaries are used as educational tools for the participants during the course of treatment to help them master dietary and behavioral skills. Interventionists will review the diaries weekly and provide feedback to reinforce or shape new behaviors

and to identify high risk situations for problem solving. Participants will be encouraged to continue self-monitoring as a behavioral strategy to control food intake throughout the 18 month program. However, after the first 6 months, feedback on self-monitoring will be provided monthly rather than weekly.

The skills required to make appropriate dietary changes will be modeled, practiced and reinforced throughout the program. Participants will be trained to use the behavioral strategies to implement the recommended dietary changes. Additionally, in order to make our website dynamic, we will post weekly nutrition and diet facts, helpful hints, local restaurant information, etc.

Exercise. The same exercise recommendations will be provided to both intervention conditions and will reflect the recommendations that the investigative team has used in their previous weight loss trials. Participants will be provided with graded goals to reach the recommended weekly minimum of 200 minutes of moderate intensity exercise by week 9 of the program. This magnitude of exercise has been shown to be improve in long-term weight loss in overweight adults, is the most common exercise prescription in weight loss trials, and is consistent with the recommendations from the American College of Sports Medicine. To achieve this goal, exercise will be prescribed for 5 days/wk, and this is consistent with the recent findings suggesting that this prescription will increase exercise participation compared to prescribed exercise on fewer days per week. To facilitate the adoption and maintenance of these levels of exercise, participants will be permitted to divide the exercise into multiple bouts of exercise per day that are at least 10 minutes in duration.

The preferred mode of moderate exercise will likely be brisk walking, although other forms of aerobic exercise will also be encouraged should the participant prefer an alternative mode of exercise or a variety of exercise experiences. All exercise will be monitored using electronic diaries or apps that include pull down menus for a wide range of activities and provide calculations for the number of calories expended based on the activity and number of minutes reported. Participants are asked to record the type of activity, the number of minutes and the calories expended. A pedometer or other wearable electronic physical activity tracker will be provided to each participant to assist in increased physical activity.

Behavioral Strategies. Behavioral strategies to develop new habits and behavior patterns and sustain them are the foundation of the intervention approach. Specifically, self-monitoring, goal setting, problem solving, relapse prevention and social support will be emphasized in the intervention. Participants will self monitor their dietary intake and physical activity electronically and will receive feedback from the counselor to fine tune their dietary change efforts. Goal setting is emphasized in each session, with short term goals and long term goals identified to sustain motivation while building confidence and self efficacy and fostering appropriate expectations. Web features that encourage social support include the bulletin board for sharing supportive comments as well as pictures posted on the secure website to allow a more “virtual group” experience. Group competitions that put groups into teams to develop social support are used to promote social support. For example, competitions to see which groups can achieve the best attendance or number of steps taken in the previous week with small incentives

available to the team which achieves the goal (such as a cookbook, exercise equipment, or gift cards to obtain similar items).

Daily self-weighing has been associated with successful long-term weight control success and therefore this self regulation strategy will be recommended in the current program. A digital scale will be provided to each participant to assure that everyone has access to this important tool.

Internet Delivery of a Behavioral Weight Control Program

Access to the lessons and other study materials will be username and password protected to ensure that no individuals from outside the study access the website and that participants can only access the intervention materials from their own group and their own personal data. Participants will be enrolled into a virtual "group" which will be maintained throughout study participation although they never meet in person. After the weight loss induction phase is completed (week 24), online chat sessions will be reduced to once a month but all other components of the website will remain available to participants. Individual usage of the website will be tracked by username through server activity logging.

Participation in the weekly chats and self monitoring of diet and physical activity behaviors is estimated to require 5 hours weekly. After the weekly sessions transition into monthly sessions, there will no longer be the requirement for weekly self monitoring but continued regular self monitoring will be strongly encouraged as it is associated with successful long-term weight maintenance.

Economic Incentives Condition

All participants will be asked to self monitor their weight daily, as well as record their dietary intake and physical activity electronically. This information will form the basis of the incentive algorithm that will underlie the incentive structure and allow individual determination of whether an incentive is delivered. The electronic system of data capture allows real-time determination of which incentive should be awarded each week.

Three self-management behaviors are targeted for incentives: (1) weighing daily; (2) recording foods and drink consumed; and (3) achieving a "step goal" designed to get participants more physically active. Each week, a "payout" day will be randomly selected from the previous week starting in week 2 (i.e. in week 2 a random date from week 1 will be identified). Participants who engaged in the target self-management behaviors (weighed self and reported weight, self-monitored dietary intake, and/or recorded a step total which met their tailored step goal) on that randomly selected "payout day" will receive a modest incentive ($1) for each of the three independent behaviors. If the participant engaged in the behavior on the day before the payout day, then the incentive will be doubled ($2) and if the participant engaged in the behavior on both the previous days (for a total of three days in a row), the largest payout will be received

($3). Thus, a participant who performs all three behaviors consistently has the opportunity to earn $3 for each of 3 behaviors (for a total of $9 each week) during the first 6 months of the program. Individuals who did not engage in the behavior on the randomly-selected payout day will receive no incentive. Half of the weekly payout will be posted to an Amazon.com account in the participant's name, allowing the participant immediate access to the incentive. The other half of the incentive earned that week will be deposited into a personal incentive saving account which will accrue over time. Each week additional incentives will be deposited cumulatively to the Amazon account and to the personal incentive savings account for individuals who engaged in at least 1 of the target behaviors on the payout day.

At 2, 6 and 12-month assessments, participants will be about to recoup the saving account if they have met minimal weight loss thresholds. Those individuals who have achieved substantive weight loss thresholds will be offered a bonus payout at their 2, 6- and 12-month assessment, with the bonus equaling the amount in reserve in the personal incentive savings account.

Follow-up Data Collection Visits
Participants will be alerted prior to their follow-up assessment appointments to complete the online questionnaires which are anticipated to take approximately 30 minutes to complete. They will also be scheduled to come into the clinic to get weighed, at which time the weight loss achieved will be verified (and the payout amount from the incentive savings account will be determined for those in the Internet+Incentive condition).

All participants (in both treatment conditions) will be offered small incentives such as tote bags, cookbooks, exercise equipment, etc. (valued at approximately $10-15) after completion of the follow-up data collection visits as token of appreciate for their participation.

All procedures are for research only and not part of routine care.

For research involving survey, questionnaires, etc.: *Describe the setting and the mode of administering the instrument and the provisions for maintaining privacy and confidentiality. Include the duration, intervals of administration, and overall length of participation. (describe and attach all instruments)*

☐ ***Not applicable***

Surveys and questionnaires will be administered online. Participants will be given a unique identification number and password to access the questionnaires. Participants will not have access to review the questionnaires after completion or to make changes after submitting the forms. They will be provided with a helpline contact should they encounter difficulty in completing the forms. If participants prefer, they can complete the forms using a paper copy rather than online. It is expected that the online follow-up assessment questionnaires will take less than 30 minutes to complete and the in-person follow up assessment (weighing in) will take less than 30 minutes.

Statistical Considerations: *Delineate the precise outcomes to be measured and analyzed. Describe how these results will be measured and statistically analyzed. Delineate methods used to estimate the required number of subjects. Describe power*

calculations if the study involves comparisons. Perform this analysis on each of the primary and secondary objectives, if possible.

Sample Size and Power Calculations. The primary analysis compares percent weight loss from baseline to 6-month in the Internet+Incentive condition with the Internet alone condition. Weight loss estimates for Internet alone are 5.8 kg based on 6-month data from our current Internet trial. The incremental weight loss effect expected is 2.2 kg based on the work of Dr. Leahey, which demonstrated a 2.2 kg greater weight loss among individuals randomized to an online behavioral self-help program plus incentives than the weight losses achieved by individuals given the online self-help program only. Thus, we expect average weight losses of 8 kg in the Internet+Incentive condition. The corresponding estimate of the standard deviations for weight loss at 6 months for the Internet + Incentive condition and the Internet alone condition is SD = 5.8kg. Since the design uses randomization of fixed number of participants to the two conditions, sample size and power calculations need to consider the possibility of a clustering effect among participants. A conservative ICC value of 0.05 was used to reflect our current iREACH data. The inflated variance estimate for the 6-month weight loss assuming a set of 16 participants in each wave becomes $(5.8)^2$ [1 + (16-1) 0.05] = $(7.67 \text{ kg})^2$. A one-way fixed effect analysis of variance approach with a 5% Type I error level indicates that a total of 177 participants per condition (354 total) will be required to allow for a 80% power to detect the condition effect sizes above. We conservatively project 10% attrition at 6-months and 15% at 18-months (which is inflated over our actual experience in iREACH in which we obtained primary outcomes on 98% at 6 months and 92% at 18-months) and thus will need to randomize 208 participants per condition. Therefore, we propose to enroll 416 participants equally across two sites (Vermont and South Carolina).

Statistical Analysis. Dr. Taka Ashikaga, Director of the UVM College of Medicine Bioinformatics Facility, will supervise the data management and the statistical analysis, as he has for the past two iREACH trials. Data management will follow standardized protocols for data entry, review and verification. The primary hypothesis examining weight loss outcomes over time will be addressed using a mixed model implementing a repeated measures analysis of variance with site and treatment condition as the between group factors and assessment time (2, 6, 12, and 18 months) as the within subject factor recalling that the baseline value will be subtracted from all subsequent values. An intent-to-treat approach will be used as the definitive analysis perspective for both the primary hypothesis testing and the secondary analysis of data. The use of a multiple imputation process will be conducted if the missing data can be assumed to be missing at random or completely at random. The intent-to-treat approach will require the use of a mixed model approach that can deal with repeated measures data and which can also deal with missing data (e.g. SAS ProcMixed or BMDP5V). Multiple imputed samples will be generated using SAS ProcMI and these multiple samples examined to determine the robustness of the overall intent-to-treat results with results generated from imputation modeling. These two approaches will be followed by the examination of group effects using completer data only. Results using all three perspectives will be compared for major qualitative differences in the conclusions. The relationship between treatment engagement factors (e.g., attendance, self-monitoring, self-weighing, as well as changes in diet, exercise, and motivation) and weight loss with possible confounding variables will also be examined using a mixed model of the repeated measures where the confounding variables will be treated as time dependent covariates. Similar analysis models will be developed for the 5% and 10% weight loss outcomes using mixed models with a logit link function to deal with these dichotomized measures. A supplement to the general mixed model approach will be taken and will include the use of a hierarchical regression analysis model perspective where regression coefficients characterizing the

temporal courses of individual weights at all time points, and diet information and exercise levels, will be parameterized as random coefficients that will be examined as functions of group assignment and degree of adherence to treatment protocols. These hierarchical regression analyses will also allow for use of participants who do not complete the full set of observational time points.

Economic Analyses. To quantify the incremental cost-effectiveness of the Internet+Incentive intervention, we will adopt economic costing methods that Dr. Finkelstein has employed previously.[104,105] We will compare the difference in costs to the difference in effectiveness. The primary difference in costs will be the incentive payouts. The difference in effectiveness will be presented both in terms of incremental change in weight and change in QoL scores, as measured by the EQ5D. We will then simulate potential long-term cost-effectiveness ratios under various assumptions about the sustainability of any improvements in QoL beyond the trial duration. Dr. Finkelstein, study consultant, successfully applied this approach in a forthcoming manuscript documenting the incremental cost-effectiveness of commercially available non-surgical weight loss interventions.

Randomization. The College of Medicine Bioinformatics Facility Interactive Voice Response (IVR) system will be used to randomize groups of individuals to treatment condition. Dr. Ashikaga will access the IVR system and will use distributional characteristics of the baseline BMI of the intact groups to randomize to achieve between treatment arm balance. The current iREACH study has utilized the 25th, 50th and 75th percentiles of each intact group and has been successful in allocating groups to treatment conditions with little variation between groups compared to within group variation.

Confidentiality Measures and Secure Storage of Data or Tissue: *Describe how the data/tissue will be collected. Will there be identifiers or will the data/tissue be coded? Describe where the data/tissue will be stored and how it will be secured. Describe who will have access to the data/tissue or the codes. If subject data/tissues with identifiers will be released, specify to whom. Describe what will happen to the data/tissues when the research has been completed.*

☐ ***Not Applicable***

Every effort will be made to keep participants' information private and confidential. Confidentiality will be ensured by coding data with a unique ID number, and all data collected will be stored in locked files with access restricted to study personnel, and password protected computer data files. Participants will not be personally identified in any scientific reports generated by the study or any other dissemination efforts. All results will be presented in aggregate form. All project staff will undergo training and ongoing continuing education about methods to protect confidentiality.

Storage of Collected Data. All paper data will be stored in a locked file cabinet, and all electronic data will be stored in password-protected files. Data will only be accessed when coded, entered, or audited. The study's Project Coordinators will work closely with the UVM Bioinformatics facility to ensure the secure storage of all project questionnaires and electronic data, using appropriate data safety procedures. Site specific data will be sent to the Statistician, Dr. Ashikaga, using secure FTP transfers. All original transferred data files will be stored on a dedicated PC with limited and secured password protected access in a private locked office. Data management and editing of these files will take place prior to archiving any data files into a SAS based project specific database with specific

documentation of any editing and data review adjudications while the original data files will be retained intact. Only archived data files will be used to derive analysis data files to address specific hypotheses or project monitoring reports.

The data entry system will require a login identification and password in order to gain access to the data. Where appropriate, validation and range rules will be applied to the actual entry field. Only the Bioinformatics Staff will be able to view the data in its raw state. All other authorized personnel (Principal Investigators, Research Assistants, and Project Coordinators) will view data via forms and reports created by the Bioinformatics Staff.

Risks/Benefits: *Describe any potential or known risks. This includes physical, psychological, social, legal or other risks. Estimate the probability that given risk may occur, its severity and potential reversibility. If the study involves a placebo or washout period, the risks related to these must be addressed in both the protocol and consent. Describe the planned procedures for protecting against or minimizing potential risks and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to the subjects are reasonable in relation to the anticipated benefits to subjects and others. Discuss the importance of the knowledge gained or to be gained as a result of the proposed research and why the risks are reasonable in relation to the knowledge that reasonably may result. If there are no benefits state so.*

Potential Risks. No social, legal or other risks are anticipated as part of this project. All assessment procedures and intervention recommendations have been used in previous studies without adverse outcomes. Assessment methods reflect procedures that individuals might encounter in a routine health care visit (i.e., weight assessment) or questionnaire measures that have been implemented in numerous studies without difficulties (e.g., dietary intake and physical activity questionnaires).

Intervention methods are similarly very low risk. Behavioral weight control interventions recommend that individuals make changes to dietary intake and physical activity, all of which are comparable to the recommendations made by national advisory panels and recognized leaders in health recommendations. Specifically, the intervention goals outlined are consistent with NHLBI recommendations, the American Heart Association, the American Diabetes Association, etc. These intervention recommendations for diet and activity habit change have minimal risk. The most common risk associated with participation in the interventions is soreness or musculoskeletal injury, although this occurs infrequently. Precautions will be taken to further minimize risk by making recommendations for graded increases that slowly increase activity duration and frequency and appropriate stretching. Moderate exercise prescriptions rather than vigorous levels of physical activity should also minimize these risks.

A potential risk in the present study is that participants may fail to lose weight in the program, but this risk occurs in all approaches to weight control. Alternative approaches to weight loss, including stricter diets, pharmacological interventions, and surgical procedures, are considered to have greater risk than the dietary and physical activity program described in this protocol. Participants may utilized unhealthy dietary practices to lose weight and/or may experience minor musculoskeletal injuries during exercise; however, this is considered unlikely and precautions will be taken to further minimize this risk.

Protection Against Risk. Every effort will be made to keep participants' information private and confidential. Confidentiality will be ensured by coding data with a unique ID number, and all data collected will be stored in locked files with access restricted to study personnel, and password protected computer data files. Participants will not be personally identified in any scientific reports generated by the study or any other dissemination efforts. All results will be presented in aggregate form. All project staff will undergo training and ongoing continuing education about methods to protect confidentiality.

Participants will be taught warm-up and stretching techniques to precede all exercise sessions to minimize the chance of muscle injury. In addition, weekly self-monitoring diaries will be submitted and reviewed at regular intervals throughout the study allowing for assessment of nutritional adequacy. No calorie goals will be set below 1000-1200 kcal/day to provide participants with sufficient calories for a nutritionally adequate diet. Participants who become pregnant during the course of the 18-month study will be dropped from the treatment protocol, and participants who experience other medical problems during the course of the study will be referred to their personal physician for care as appropriate.

Potential Benefits of the Proposed Research to Human Subjects and Others. The potential benefit to the participants will be the skills and knowledge in lifestyle behaviors to successfully lose weight and prevent/deter weight re-gain. Further, participants may benefit from the improved health and psychological well-being that commonly accompanies weight loss. These benefits to the individual participant are considered substantial. If as effective as expected, the results of this study could demonstrate a more successful and/or cost effective approach to weight control which has the potential to be more broadly disseminated and have greater reach than current approaches, and thus the benefit to society would also be great.

Importance of Knowledge to be Gained. Obesity is one of our most pressing public health problems largely because produces or exacerbates a wide range of chronic diseases. Behavioral weight control programs that successfully achieve weight losses and improvements in associated obesity-related co-morbidities have been developed and demonstrated efficacious. However, due to lack of proximity to evidence-based weight management programs and time constraints, access and adherence to these beneficial programs may be limited. Development of new weight control technologies that utilize the Internet may reduce some of these treatment barriers. The knowledge gained in this study will contribute evidence necessary to inform the development of more successful, cost-effective Internet-based approaches to weight control.

Therapeutic Alternatives: *List the therapeutic alternatives that are reasonably available that may be of benefit to the potential subject and include in the consent form as well.*

☐ ***Not Applicable***

There are a variety of weight loss programs available as a therapeutic alternative. Individuals can join commercial programs or speak with their physician to get assistance with their weight loss efforts. In addition, pharmacological interventions, and surgical procedures that produce weight loss are available, if deemed appropriate by the individual's physician.

Data Safety and Monitoring: *The specific design of a Data and Safety Monitoring Plan (DSMP) for a protocol may vary extensively depending on the potential risks, size, and complexity of the research study. For a minimal risk study, a DSMP*

could be as simple as a description of the Principal Investigator's plan for monitoring the data and performance of safety reviews or it could be as complex as the initiation of an external, independent Data Safety and Monitoring Board (DSMB). The UVM/UVM Medical Center process for review of adverse events should be included in the DSMP.

The proposed study poses no serious physical, psychological, or legal risks to participants. Therefore, the trial will be monitored by an internal data safety monitoring committee consisting of the Principal Investigators (Jean Harvey, PhD and Delia Smith West, PhD), Project Coordinators from both states, Biostatistician (Taka Ashikaga, PhD) and interventionists who facilitate the group chats. Weekly meetings or conference calls will be held to evaluate the status of study participants. Any serious adverse events will be recorded on a standard form and reported to the respective project coordinator, to the PI of both clinical centers, and the IRB at both institutions [the University of Vermont Committee on Human Subjects in the Medical Sciences (CHRMS) and the University of South Carolina Institutional Review Board]. The NIH will be informed of serious adverse events and any actions taken unless the committee or the IRB at either institution recommends that the NIH be informed sooner.

Adverse Event and Unanticipated Problem (UAP) Reporting: *Describe how events and UAPs will be evaluated and reported to the IRB. All protocols should specify that, in the absence of more stringent reporting requirements, the guidelines established in the Committees on Human Research "Adverse Event and Unanticipated Problems Reporting Policy" will be followed. The UVM/UVM Medical Center process for review of adverse events and UAPs to subjects or others should be included in the DSMP.*

The guidelines established in the Committees on Human Research "Adverse Event and Unanticipated Problems Reporting Policy" will be followed.

Withdrawal Procedures: *Define the precise criteria for withdrawing subjects from the study. Include a description of study requirements for when a subject withdraws him or herself from the study (if applicable).*

Participants may withdraw from the study at any time by notifying the PI or Study Coordinator in writing (or by email) of their intention.

If necessary, subjects may be terminated or withdrawn by the Principal Investigator without the consent of the participant if continued participation would be contraindicated, including because the participant (1) becomes pregnant (and therefore it would not be appropriate to follow a weight loss program); (2) develops a life threatening disease for which weight loss is contraindicated; (3) joins another weight control program (such as Weight Watchers, Jenny Craig, NutriSystems, etc.); or (4) the participant moves more than 120 miles from the clinical center with no plans to return during study assessment windows.

Sources of Materials: *Identify sources of research material obtained from individually identifiable human subjects in the form of specimens, records or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records or data.*

The anthropometric, behavioral, economic and self-report questionnaire data collected in this study will be obtained for research purposes only

DRUG AND DEVICE INFORMATION

Investigators are encouraged to consult the UVM Medical Center Investigational Pharmacy Drug Service (847-4863) prior to finalizing study drug/substance procedures.

Drug (s) [x] ***Not applicable***

Drug name – generic followed by brand name and common abbreviations. Availability – Source and pharmacology; vial or product sizes and supplier. If a placebo will be used, identify its contents and source. (attach investigational drug brochure)

Preparation: Reconstitution instructions; preparation of a sterile product, compounded dosage form; mixing guidelines, including fluid and volume required. Identify who will prepare.

Storage and stability – for both intact and mixed products.

Administration – Describe acceptable routes and methods of administration and any associated risks of administration.

Toxicity – Accurate but concise listings of major toxicities. Rare toxicities, which may be severe, should be included by indicated incidence. Also adverse interactions with other drugs used in the protocol regimen as well as specific foods should be noted. Address significant drug or drug/food interactions in the consent form as well. List all with above details.

Is it FDA approved: (include FDA IND Number)

1. *in the dosage form specified? If no, provide justification for proposed use and source of the study drug in that form.*
2. *for the route of administration specified? If no, provide justification for route and describe the method to accomplish.*
3. *for the intended action?*

Device (s) [x] ***Not applicable***

Device name and indications (attach investigational device brochure)

Is it FDA approved: (include FDA IDE Number)

1. for indication specified? If no, provide justification for proposed use and source of the device.

Risk assessment (non-significant/significant risk) - PI or sponsor needs to assess risk of a device based upon the use of the device with human subjects in a research environment.

SUBJECT CHARACTERISTICS, IDENTIFICATION AND RECRUITMENT

Subject Selection: *Provide rationale for subject selection in terms of the scientific objectives and proposed study design.*

This is a comparative efficacy trial. Therefore, subjects are selected to provide a sample of individuals likely to engage in the interventions offered to allow testing of the two interventions proposed. Towards this end, only individuals with pre-existing technology that will allow access to the intervention delivery (specifically, access to Internet on desktop computer and a smartphone) will be eligible. The study does not seek to introduce use of this technology to naïve users who have no daily access. Furthermore, potential participants will be required to demonstrate some ability to comply with study intervention procedures to be eligible (specifically, they must complete an online dietary self-monitoring diary for 1 week and log on for a brief chat) so that only adequately motivated individuals who are likely to stay engaged for the full 18 month study period are enrolled and randomized.

Vulnerable Populations: *Explain the rationale for involvement of special classes of subjects, if any. Discuss what procedures or practices will be used in the protocol to minimize their susceptibility to undue influences and unnecessary risk (physical, psychological, etc.).*

x	***Not applicable***

Number of Subjects: *What is the anticipated number of subjects to be enrolled at UVM/UVM Medical Center and in the case of a multi-center study, with UVM/UVM Medical Center as the lead, the total number of subjects for the entire study.*

A total of 416 participants will be recruited to participate in the study, with half the cohort recruited from Vermont (VT) and half from South Carolina (SC). Given the demographic patterns within these two states, we anticipate that most minority participants will be recruited at the SC site.

Inclusion/Exclusion Criteria: *Eligibility and ineligibility criteria should be specific. Describe how eligibility will be determined and by whom. Changes to the eligibility criteria at a later phase of the research have the potential to invalidate the research.*

To be eligible to participate, participants must be at least 18 years old and have a BMI (kg/m^2) between 25 and 55. Individuals must also be free of medical problems that might contraindicate participation in a behavioral weight reduction program containing an exercise component, not currently on medication that

might affect weight loss, not currently pregnant or pregnant in the previous 6 months or currently breastfeeding, and not enrolled in another weight reduction program (all of which would be problematic confounds for the primary outcome of body weight). All participants must have a computer (at home or work) with access to the Internet and a smart phone (to allow use of step counting apps). Only one member of a household will be eligible to participate. Participants must successfully complete a self-monitoring diary of foods consumed for a week (as a measure of likelihood of adhering to the program requirements), demonstrate the ability to access the website successfully (practice chat) and agree to be randomized in order to be eligible.

Individuals will be considered ineligible if they have had a heart attack or a stroke in the past 6 months, have ever had weight loss surgery, have lost more than 10% of body weight in the previous 6 months, are currently taking medications for weight loss, or are required by their doctor to follow a special diet (other than a low fat diet). Individuals who indicate plans to move from the area in the upcoming 18 months or who have schedules that will make it likely that they will have difficulty attending the scheduled "chat" groups will also be considered ineligible.

Inclusion of Minorities and Women: *Describe efforts to include minorities and women. If either minorities or women are excluded, include a justification for the exclusion.*

Neither minorities nor women are excluded. The gender composition of the sample is anticipated to resemble that of most obesity treatment studies and the volunteers who participated in our previous. We expect approximately 80-90% women. Further, based on our previous experiences in iREACH we expect that at least 25% of our sample will be drawn from minority populations. We will over-sample from among minority groups given the substantial health disparities that surround obesity, diabetes and other CVD risk factors in these populations.

Inclusion of Children: *Describe efforts to include children. Inclusion is required unless a clear and compelling rationale shows that inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. If children are included, the description of the plan should include a rationale for selecting or excluding a specific age range of children. When included, the plan must also describe the expertise of the investigative team in working with children, the appropriateness of the available facilities to accommodate children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.* ***If children are excluded*** *then provide appropriate justification. Provide target accrual for this population.*

We propose to exclude children below age 18 because the proposed behavioral weight control intervention has not been studied in children. Effective behavioral obesity treatment for children requires appropriate adaptation for their developmental needs. Thus, the current intervention approach may not be appropriate for younger children. However, children aged 18 to 21 years will be eligible to participate.

For protocols including the use of an investigational drug, indicate whether women of childbearing potential have been included and, if not, include appropriate justification.

N/A

If HIV testing is included specifically for research purposes explain how the test results will be protected against unauthorized disclosure. Include if the subjects are to be informed of the test results. If yes, include the process and provision for counseling. If no, a rationale for not informing the subjects should be included.

x	***Not applicable***

N/A

Recruitment: *Describe plans for identifying and recruitment of subjects. All recruitment materials (flyers, ads, letters, etc) need to be IRB approved prior to use.*

Our recruitment approach is multi-faceted and reflects our successful experience enrolling target recruitment goal in the previous two internet assisted obesity treatment programs. We propose to extend this approach to the current project. Participants will be recruited through: (1) direct, community-based efforts using large media (newspaper ads, radio notices, television features, etc.) and small media (internet postings, brochures in local businesses, talks to local community, notices in churches, local newsletters, etc.); (2) targeted emails using available distribution lists likely to have potentially eligible individuals (e.g., teachers union memberships, university mailings, and employers, etc.); and (3) direct recruitment materials placed in the offices of physicians (specifically in primary care settings). Interested persons will be directed to a secure online recruitment webpage which queries for basic contact information and eligibly criteria (self-reported height and weight, age, etc.) and provides additional information regarding the study. Individuals who appear likely to be eligible based on this online registration will receive a brief phone screen conducted by research staff to confirm initial eligibility for the study and will be scheduled for an in-person orientation session where the study will be reviewed in detail, questions will be addressed and an informed consent document will be provided to take home. After considering the study for a minimum of 1 week, interested participants will be asked to sign a consent form at the first baseline data collection visit. Consent forms will have been approved by the Institutional Review Board of the respective institution at which the subject is being recruited, either the University of Vermont or the University of South Carolina, as appropriate.

FINANCIAL CONSIDERATIONS

Expense to Subject: *If the investigation involves the possibility of added expense to the subject (longer hospitalization, extra studies, etc.) indicate in detail how this will be handled. In cases where the FDA has authorized the drug or device company to charge the patient for the experimental drug or device,* ***a copy of the authorization letter from the FDA or sponsor must accompany the application. Final approval will not be granted until the IRB receives this documentation.***

There are very limited circumstances under which study participants may be responsible (either directly or via their insurance) for covering some study-related expenses. If the study participant or their insurer(s) will be billed for any portion of the research study, provide a justification as to why this is appropriate and acceptable. For example, if the study involves treatment that is documented standard of care and not investigational, state so. In these cases, the protocol and the consent should clearly define what is standard of care and what is research.

No additional expense to participants is anticipated, and no proposed research procedures will be billed to participants.

Payment for participation: *Describe all plans to pay subjects, either in cash, a gift or gift certificate. Please note that all payments must be prorated throughout the life of the study. The IRB will not approve a study where there is only a lump sum payment at the end of the study because this can be considered coercive. The amount of payment must be justified. Clarify if subjects will be reimbursed for travel or other expenses.*

☐ ***Not applicable***

Participants randomized to the Internet+Incentives intervention arm will have the opportunity to earn payment in the form of gift cards based on their self-monitoring of weight management behaviors (body weight, dietary intake and physical activity in the form of number of steps taken. These behaviors are consistently and robustly associated with successful weight loss, and also theoretically important from a self-regulation perspective. Incentives can also be "earned" by meeting weight loss thresholds at the data collection visits. A maximum of $590 can be "earned" in a 12 month period for participants who participate at the highest level and are fully adherent to self-monitoring recommendations and who achieve and sustain 10% weight loss, although it is estimated that this is unlikely that many participants will achieve this level of adherence. No incentives can be earned during months 12-18 of participation; all incentive potential is in the first year of participation. The incentives will be delivered weekly by electronic delivery with weekly amounts of a maximum of $9. *These financial incentives are a key element of the scientific questions being evaluated and are integrated into the treatment approach, and thus are considered as part of the intervention.*

Participants will also be offered small tokens for attending data collection visits. Items such as tote bags, cookbooks, exercise videos, etc. (value of $10-15) will be provided to those who provide follow-up data.

Collaborating Sites*. When research involving human subjects will take place at collaborating sites or other performance sites when UVM/UVM Medical Center is the lead site, the principal investigator must provide in this section a list of the collaborating sites and their Federalwide Assurance numbers when applicable. (agreements may be necessary)*

☐ ***Not applicable***

Two clinical sites are engaged in this research. In addition to UVM (Dr. Harvey PI), University of South Carolina, Columbia, SC is a collaborating site, directed by the other PI (multiple PIs) Dr. West. The Federalwide Assurance number for University of South Carolina is 00000404. Approval of the University of South Carolina Institution Review Board will be obtained prior to engaging in any recruitment, data collection or intervention activities at either site.

INFORMED CONSENT

Consent Procedures*: Describe the consent procedures to be followed, including the circumstances under which consent will be obtained, who will seek it, and the methods of documenting consent. Specify the form(s) that will be used e.g. consent (if multiple forms explain and place identifier on each form), assent form and/or HIPAA authorization (if PHI is included). These form(s) must accompany the protocol as an appendix or attachment.*

Note: Only those individuals authorized to solicit consent may sign the consent form confirming that the prospective subject was provided the necessary information and that any questions asked were answered.

Interested persons will be directed to a secure online recruitment webpage which queries for basic contact information and eligibly criteria (self-reported height and weight, age, etc.) and provides additional information regarding the study. Individuals who appear likely to be eligible based on this online registration will receive a brief phone screen conducted by research staff to confirm initial eligibility for the study and will be scheduled for an in-person orientation session. During the orientation designated staff who has been certified to obtain consent will discuss the informed consent form with the subject volunteer, reviewing each aspect of the consent form and allowing individuals to ask questions. This orientation may be delivered in a group setting, although if scheduling does not permit engaging in the group orientation, the subject volunteer may be orientated individually. Subject volunteers often benefit from the group process in that they hear questions that others ask which may not have occurred to them but are of interest to them in their decision making about participation. Subject volunteers will be provided with a copy of the consent form at the group orientation but will not be asked to sign the form until they return for an individual visit. Individuals who remain interested in the study after the orientation session and have reviewed the consent form will be invited to return for an individual screening session at which the remainder of the consent process will occur. The consent process will take place in a quiet and private room. The person obtaining consent at this visit will be an individual who has been certified to obtain consent for the study and this person will thoroughly explain each element of the document and outline the risks and benefits, alternate treatment(s), and follow-up requirements of the study. Participation privacy will be maintained and questions regarding participation will be answered. No coercion or undue influence will be used in the consent process. No research related procedures will be performed prior to obtaining informed consent. All signatures and dates will be obtained. A copy of the signed consent will be given to the participant. The informed consent process will be documented in each subject's research record.

Following informed consent, the remainder of screening will be conducted (e.g., self monitoring diary completed, discussion of randomization acceptance) and baseline data will be collected. Only those individuals with complete baseline data will be randomized.

Information Withheld From Subjects: *Will any information about the research purpose and design be withheld from potential or participating subjects? If so, explain and justify the non-disclosure and describe plans for post-study debriefing.*

x	***Not applicable***

Attach full grant application, including budget information and/or any contract or draft contract associated with this application.