This supplement contains the following items:

1. Original protocol, final protocol, summary of changes
2. Statistical Analysis Plan
1. EXECUTIVE SUMMARY

Young adults, aged 20-35 years, experience the greatest rate of weight gain, averaging 1-2 lbs/yr. Over time, this weight gain is associated with a worsening in cardiovascular disease risk factors and an increase in the prevalence of metabolic syndrome. Given the difficulties in producing sustained weight loss later in life, preventing weight gain from occurring during this critical period is key to curbing the obesity epidemic. The Study of Novel Approaches for Prevention (SNAP) is a 2-center randomized trial designed to test whether behavioral interventions based on self-regulation can prevent weight gain in young adults (18-35 years; body mass index (BMI) 21-30 kg/m²). Approximately 600 participants will be recruited over two years and randomly assigned to control (N=200), self-regulation with small changes (N=200) or self-regulation with large changes (N=200). The Small Changes group will be taught to make small, consistent, changes in eating and exercise behavior to prevent weight gain or reverse weight gain if it occurs whereas the Large Changes group will emphasize periodic, larger changes in eating and exercise, with a goal of producing weight loss and thereby providing a buffer against anticipated weight gain. The primary aim of the trial is to test whether the magnitude of weight gain from baseline across an average planned follow-up of three years differs across the three groups, with a priori hypotheses that weight gain will be greater in the Control group than in either intervention and greater in the Small Changes than Large Changes group. Secondary aims are to compare the three groups over the planned follow-up on a) the proportion of participants in the three groups who gain less than 1 pound, b) the changes in behaviors and psychosocial measures (diet, physical activity, dietary restraint, frequency of self-weighing, depression, and occurrence of abnormal eating behaviors), and c) the changes in cardiovascular disease risk factors (blood pressure, lipids, insulin sensitivity, and waist circumference). The trial will also examine the association among changes in behaviors, weight, and cardiovascular disease risk factors and examine variables that may moderate the effects of the intervention (including gender, ethnicity, initial BMI, age) and potential mediators of the effects of the intervention (including changes in diet, activity, and self-regulatory behaviors).

2. BACKGROUND

Recent studies have shown that individuals who have favorable cardiovascular risk profiles as young adults have very low long-term risk of cardiovascular disease and longer survival. In a study of over 7300 women, only 20% had a favorable cardiovascular disease risk profile at age 18-30 (including BMI <25 kg/m², normal blood pressure, normal lipid levels, not smoking and no diabetes). However, in this 20%, coronary heart disease and cardiovascular disease were very rare. Over a 31-year follow-up, the multivariate adjusted cardiovascular disease mortality hazard ratio for low risk women was 0.19 compared with women with two or more high risk factors. Other studies have confirmed the benefits of having optimal levels of cardiovascular disease risk factors at young and middle age, and shown that those with optimal risk profiles report better quality of life, lower medication use and prevalence of clinical diseases, and lower average annual health care costs in older age. These findings emphasize the need to prevent the development of adverse risk factors in young adults.
A key factor associated with the worsening in cardiovascular disease risk factors in young adults is weight gain. The Coronary Artery Risk Development in Young Adults (CARDIA) Study, which followed over 3,300 black and white men and women, showed that young adults have an average weight gain of 15 kg over 15 years. Only 16.3% maintained a stable BMI over the 15 years, but individuals who remained weight stable had essentially unchanged levels of all of the components of the metabolic syndrome, regardless of their initial body mass index, age, race, or gender. In contrast, those who gained weight had worsening in cardiovascular risk factors and increased prevalence of the metabolic syndrome. These studies suggest that an important public health approach to preventing heart disease in later life would be to prevent weight gain, and the associated worsening in risk factors, during young adulthood.

Targeting young adults for weight gain prevention is important not only to prevent the increase in cardiovascular disease risk factors in the young adults themselves, but because it may also reduce the risk of obesity among offspring. Parent obesity level is among the strongest independent predictor of weight status in children. With the average maternal age of first childbirth in the U.S. at 25 years, preventing weight gain during this high-risk period and beyond may have a positive ripple effect on childhood obesity as well.

To date, there has been no intervention that has been shown in a rigorously conducted randomized controlled clinical trial to be successful in preventing long-term weight gain in young adults. SNAP will test two interventions for use in young adults. These interventions will both be based on the theory and principles of self-regulation. Self-regulation was the core of STOP Regain, our weight loss maintenance program that prevented weight regain over an 18-month period. In STOP Regain, participants were asked to weigh themselves daily, compare their weight to a goal weight (weight at the start of the program), and then depending on the correspondence between the two, either making adjustments in eating and exercise behaviors or provide self-reinforcement. In addition, since there is little external reinforcement for maintenance of body weight, we also included a system for reporting weights, thereby increasing accountability, and periodic reinforcement for continued weight loss maintenance. The importance of frequent self-weighing, the cornerstone of self-regulation, has also been supported in secondary analyses of existing prevention program. In a reanalysis of data from the Pound of Prevention study, Linde et al. reported that those individuals who reported weighing themselves daily lost weight over 1 or 2 years follow-up, whereas those who weighed less frequently than daily experienced weight gains. Importantly, only 9% of young adults enrolling in a weight gain prevention intervention report weighing daily at baseline. Given that so few young adults weigh themselves daily, we believe that extending our successful work on self-regulation to this age group is a critical aspect of weight gain prevention during this high-risk period.

Two different self-regulation interventions for weight gain prevention will be compared in this trial—one intervention will focus on making small, consistent, changes in eating and exercise behavior to prevent weight gain or reverse weight gain if it occurs, whereas the other will emphasize larger changes in eating and exercise that occur periodically, with a goal of producing weight loss and thereby providing a buffer against anticipated weight gains. Evidence for the small changes approach comes from the theoretical papers and empirical studies of Hill and
colleagues, suggesting that increases in activity of 100 kcal per day and decreases in intake of 100 kcal per day should be sufficient to prevent weight gains of 1 to 2 pounds per year. Behavioral theory also suggests that such small changes (i.e. gradual shaping of new behaviors with small incremental changes toward a goal) should be easier to initiate and maintain than larger behavior changes since they represent less drastic modifications in behavior. SNAP will target the behaviors that appear most problematic for this age group, including soda and fast food consumption and sedentary activities.

The other approach will focus on periodic prescription of larger behavior changes designed to produce weight loss. This approach was shown to be effective in the Women’s Healthy Lifestyle Project (WHLP), a study of women during the menopause that actually succeeded in preventing weight gain and the worsening in cardiovascular disease risk factors over a period of 5 years. Women in the intervention group of WHLP participated in an initial behavioral intervention designed to produce a 5-15 pound weight loss as a means of counteracting the weight gains expected with aging. The intervention group lost an average of 0.2 lbs over the 5-year intervention whereas the assessment only group gained 5 pounds on average. The intervention group also had significantly smaller increases in LDL-cholesterol, triglycerides, glucose and waist circumference. Theoretically these larger behavior changes should be easier to implement because they yield greater immediate reinforcement from the resulting weight loss and in addition provide an opportunity for participants to practice the skills they might need to use if they experience weight gains in the future. Prior research by Tate and Wing indicate their ability to produce weight loss in young adults (average of 7 pounds in a 6 month Internet weight loss program and 14.7 pounds after 6 months in a face-to-face program), supporting the feasibility of this approach as a weight gain prevention strategy in young adults.

Although there is evidence supporting the use of a self-regulation model and suggesting potential benefits to small and large behavior change approaches, this study will be the first trial to compare these interventions and evaluate their efficacy, relative to a Control group, in the prevention of weight gain in young adults.

3. OVERVIEW OF TRIAL DESIGN

3.1 Trial Design

SNAP is a 3-armed randomized controlled clinical trial, comparing a self-regulation plus small behavior changes intervention, a self-regulation plus large behavior changes intervention, and a control condition on magnitude of weight gain over an average follow-up of 3 yrs. The trial targets enrolling 600 adults (300 at Miriam Hospital and 300 at the Univ. of North Carolina), aged 18-35 years with a BMI of 21-30 kg/m². These participants will be randomly assigned to one of three groups:

1) Control (N=200)
2) Self-regulation with small behavior changes (N=200)
3) Self-regulation with large behavior changes (N=200)

Both self-regulation interventions will include an initial 4-month program and annual booster programs extending for up to three years. Participants will be enrolled over 2 years and will be
followed from the time of randomization until the end of the grant, resulting in a planned 2-4 years of follow-up (mean of 3 years).

3.2 Specific Aims

The primary hypothesis of SNAP is that the magnitude of weight gain across an average planned follow-up of three years will differ among the three arms. Specific a priori hypotheses are that over an average of three years:

1. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus small behavior changes intervention compared to the control group.
2. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to the control group.
3. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to those assigned to the self-regulation plus small behavior changes intervention.

Secondary aims of SNAP are:

1. To compare the proportion of participants in the three groups (self-regulation plus small changes, self-regulation plus large changes, and control) who gain less than 1 pound over the planned follow-up of an average of three years;
2. To assess the mean differences in weight gain among intervention groups at 24 months post-randomization;
3. To compare the three groups on changes in behavior (e.g. diet, physical activity, abnormal eating behaviors, use of healthy and unhealthy weight control practices) and psychosocial measures (restraint, depression) over the average follow-up of three years;
4. To compare changes in cardiovascular disease risk factors (including blood pressure, lipids, insulin sensitivity, and waist circumference) across the three groups and examine the association of changes in cardiovascular disease risk factors with weight change and behavior changes;
5. To examine demographic and psychological variables that may moderate the effects of the interventions, including initial BMI, ethnicity, age, scores on the Eating Inventory, and treatment preference; and
6. To examine potential mediators of the effect of the interventions, including changes in diet, physical activity, restraint, and change in self-regulatory behaviors.

We will also compare the intervention groups on measures of adherence to the self-regulation interventions, including attendance at meetings and submission of weight data and participants’ reports of their satisfaction with the interventions. DNA will be collected and stored for potential future use. The potential of developing a proposal to provide for extended post-trial follow-up will be assessed during the trial.

3.3 Sample Size Justification

SNAP is designed to provide $\geq 90\%$ statistical power to detect average pairwise differences of 3.0 lbs between intervention arms; $N=600$ ($N=200$/arm) participants are projected to be sufficient for this goal. Group comparisons will be based on generalized linear models for longitudinal data.
To estimate power, longitudinal weight change data (i.e. follow-up weight minus baseline weight in pounds) were simulated using covariances from Levine, et al,\textsuperscript{13} which yielded the following covariance matrix for weight changes at years 1, 2, and 3.

Table 3.3.1 Covariance matrix for changes in weight from baseline (lbs).

<table>
<thead>
<tr>
<th>Year</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>57.09</td>
<td>40.29</td>
<td>38.46</td>
</tr>
<tr>
<td>Year 2</td>
<td>40.29</td>
<td>124.99</td>
<td>78.23</td>
</tr>
<tr>
<td>Year 3</td>
<td>38.46</td>
<td>78.23</td>
<td>112.00</td>
</tr>
</tbody>
</table>

This covariance matrix was used to simulate (N=25,000) longitudinal data sequences (from a multivariate normal distribution, assuming these covariances hold for months 4, 12, and 24 and be constant for months 36 and 48). It was assumed that differences in weight changes among groups will be achieved by 4 months and maintained thereafter and contrasted this with models in which initial differences waned by an accruing 10% and 20% per follow-up visit. A lost follow-up rate of 7.5% was applied at 4 months, an additional 7.5% at 12 months, and an additional 5%/yr thereafter.

Generalized linear models were fitted using maximum likelihood with unstructured covariance and tested whether the average weight loss over time varied among groups. Detectable mean differences in annual rates of weight gain between arms were projected, using a Bonferroni-adjustment (2-tailed significance level of 0.0167) to control for three pairwise comparisons. The accompanying table summarizes power projections for N=200/group for detecting a relative mean difference of 3.0 lbs at 4 months that is maintained or wanes over time. Also provided are power projections for relative intervention effects of 2.75 and 2.50 lbs.

Table 3.3.2 Projected Statistical Power for SNAP Trial

<table>
<thead>
<tr>
<th>Mean Treatment Effect at 4 Months</th>
<th>Statistical Power For Pairwise Comparisons: N=200/group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Constant</td>
</tr>
<tr>
<td>2.50 lbs</td>
<td>84%</td>
</tr>
<tr>
<td>2.75 lbs</td>
<td>91%</td>
</tr>
<tr>
<td>3.00 lbs</td>
<td>95%</td>
</tr>
</tbody>
</table>

How power is affected by different patterns of lost follow-up has also been explored: the above projections are reasonably robust across a range of assumptions.

SNAP will provide 90% power to detect a relative 28% reduction in the proportion of participants who gain weight over time. The statistical power afforded by N=200/group was projected by simulating strings of longitudinal data based on transition rates (to/fro weight gain) that were chosen to correspond to those reported by Levine, et al. A reasonable fit with a Markov model was achieved in which the probability of weight gain during the first 4 months was 0.25 and, for each successive interval, the probability of transitioning to weight gain among those entering the interval without current weight gain was 0.40 and the probability of transitioning to no weight gain among those entering the interval with weight gain was 0.20. While this model
may not have captured the full complexity of intra-individual patterns and correlation, it provided a good fit to the Levine data, particularly at Years 1 and 2. The model was extended through the four years of SNAP planned follow-up and generalized estimating equations (GEE) were used to project power. The intervention effect was defined as decreasing the probability of transitioning from no weight gain to weight gain by 28% and increasing the probability of transitioning from weight gain to no weight gain by 28%. From this N=200/group was projected to provide 94% power for each of the three (Bonferroni-adjusted) pairwise comparisons. A power of 72% is projected for the cross-sectional comparison of 36-month proportions.

4. STUDY POPULATION

SNAP targets the recruitment of 600 individuals who are aged 18–35 years and have a BMI of 21 – 30 kg/m². This age group was selected because young adults have the greatest risk of weight gain over time. The lower age cutoff of 18 years was selected since prior to this, many young adults are still living at home and thus are less responsible for food choices. Concerns about putative effects of the development of eating disorders are also greatest in younger students. The upper age cutoff of 35 years was selected because weight gain appears less common after this age.

The BMI range of 21 – 30 kg/m² was selected since weight gain prevention seems an appropriate message for these individuals. A BMI of 21 kg/m² was selected as the lower end of the eligibility criteria because individuals with a BMI of 21 kg/m² are able to lose 5-10 pounds and still remain within the normal weight range. (We will only recommend a 5 lb weight loss for individuals with a BMI of 21 to 24.9 kg/m² in the large changes condition, but have provided data in Appendix 1 showing that even if an individual with a BMI of 21 kg/m² loses 10 pounds, they will remain in the normal weight range). An upper cutoff of BMI=30 kg/m² was selected since individuals with BMI >30 kg/m² are considered obese, and weight loss (rather than weight gain prevention) is typically recommended for these individuals.14

SNAP has no restrictions with regard to gender, ethnicity, or race. It targets recruiting at least 25% men since both men and women are at risk of weight gain. It also targets recruiting at least 25% minorities, including African-Americans, Hispanic Americans, and American Indians since these groups are disproportionately affected by obesity and experience larger weight gains during young adulthood.3, 15

Exclusion criteria include:

1. Untreated hypertension, hyperlipidemia, or diabetes. We will advise individuals who have a fasting glucose >126 mg/dl, blood pressure levels >140/90 mmHg, or LDL-C >160 mg/dl of these values and recommend that they contact their physician. Since weight control is an appropriate initial treatment for these medical issues, these individuals can, if they receive permission from their physician, participate in the trial and the physician indicates that they will be managing these risk factors.

2. Treatment of diabetes with insulin or oral medications that may cause hypoglycemia (e.g. sulphonylureas). These individuals will be excluded due to the concerns about hypoglycemia in a weight control program.
3. Health problems which may influence the ability to walk for physical activity (e.g. lower limb amputation)
4. Health problems that may be associated with unintentional weight change or affect the safety of a weight loss program, including report of a heart condition, chest pain during periods of activity or rest, loss of consciousness, active tuberculosis, HIV, acromegaly, Cushing’s syndrome, chronic hepatitis B or C, inflammatory bowel disease requiring treatment within the past year, thyroid disease, renal disease, liver disease, hospitalization for asthma in the past year, or cancer within the past 5 years (except for non-melanoma skin cancers or early stage cervical cancer) or chronic use of steroid medication.
5. Report a past diagnosis of or treatment for a DSM-IV-TR eating disorder (anorexia nervosa or bulimia nervosa) or meet criteria for anorexia or bulimia nervosa during screening for this trial
6. Report a past diagnosis of or current symptoms of alcohol or substance dependence.
7. Currently pregnant, pregnant within the past 6 months, or planning to become pregnant within the next 6 months. These individuals may later be re-screened.
8. History of schizophrenia, manic depression, or bipolar disorder.
9. Hospitalization for depression or other psychiatric disorder within the past 12 months.
10. Have lost and maintained a weight loss of 10 pounds or more within the past 6 months or are currently participating in a weight loss program, taking weight loss medication, or have had surgery for weight loss.
11. Participation in another weight loss or physical activity study that would interfere with this study.
12. Another member of the household (or roommate) is a participant or staff member on this trial.
13. Reason to suspect that the participant would not adhere to the study intervention or assessment schedule (i.e., can’t come to group on a regular basis; will be away for more than two weeks during initial intervention phase or planning to move from the area within next year).
14. Not able to speak and understand English
15. Residence further than 30 miles from the intervention site
16. Perceived inability to attend the 2 year data collection visit
17. Does not have Internet access on a regular basis.

Individuals who endorse on the Physical Activity Readiness Questionnaire (PAR-Q)\(^\text{16}\) either joint problems, prescription medication usage, or other medical conditions that could limit exercise will be required to obtain written physician consent to participate.

5. RECRUITMENT and SCREENING

Participants will be recruited in cohorts of 60 (20 randomized to each group) at the clinical sites. The general recruitment strategy for SNAP will be to use a multi-method strategy including advertisements in local media (television, newspapers, Internet, radio, etc.), direct mailings to young adults, and site-specific recruitment at locations where the target population likely live and work. These site-specific recruitment strategies include attending local meetings of young adult groups and making presentations or providing information to target specific worksites and universities in the metropolitan area of each study site. Where possible we will seek out
opportunities to interact with local media about the general problem of weight gain in young adulthood and the long term, multi-center study that is available in the area to study the problem. We will conduct interviews and be available to local journalists to be interviewed for newspaper articles in various types of newspapers (student papers, local and regional papers etc.) or television programs.

In order to develop effective approaches for recruitment of both men and women for this trial, we have been conducting focus groups with young adults and asking specifically about recruitment messages and outlets. We will use this information to achieve our recruitment goals for men and women.

Both centers have prior experience recruiting minorities for weight loss studies. Investigators from the UNC have previously recruited successfully from several historically Black colleges in their area; investigators at the Miriam Hospital have recently conducted several weight loss programs for Latina women and developed excellent contacts within this community. For the most part, the types of strategies described above (television and direct mailings) have been found effective in recruiting minority participants. However, we will also consider advertisements in newspapers and on radio stations specifically focused on minority audiences, and recruitment efforts through local churches and community organizations.

Interested participants will be given basic information about the study by phone or via the study website and will complete an initial on-line screening form. Those who appear eligible will be further screened via phone interview and if eligible, invited to an orientation session during which the study will be reviewed in detail. The concept of random assignment will be described to the volunteers, as will the procedures for the assessment visits and the different treatment approaches given to each of the three arms of the study. Those who remain interested will be asked to review and sign the consent forms (see Appendix 2 for draft of consent forms). Participants will then have their height and weight taken to check eligibility and will be scheduled for two screening visits. While specific measures are described for each screening visit, we recognize that the sequence of measures may be modified across visits to fit with participant’s schedules and development of the most effective procedural flow. We anticipate that at the first screening visit (conducted in the fasting state), the study staff will complete a more detailed medical history, blood pressures will be assessed, and the phlebotomist will also take blood samples. Participants will be instructed in the procedures for wearing the SenseWear Pro Armbands. Successful completion of recording for at least 4 of the 7 days will be required for eligibility. Participants will also be given information about how to complete self-report questionnaires about their health habits using an Internet based system. At Screening Visit 2, which will occur within 1 month of randomization, we will obtain baseline measures of height, weight, and waist circumference, with the participant in a clinic gown. In addition, the questionnaire and SenseWear Pro arm-band data will be reviewed for completeness. The intervention and clinic staff will meet with the individual and complete a semi-structured interview in which the individual is asked to describe the purpose of the study and the various intervention groups to make certain that they understand the requirements of the trial. The interview will also include questions to assess the appropriateness of the individual for the trial and the timing of participation relative to other events in the individual’s life. Of greatest interest is making certain that the individual is willing to be randomized to any of the three
groups in the trial. Each week, the study staff will meet and review the information about the potential participants. These procedures, including the completion of several days of monitoring activity, the interview, and the staff review of potential participants, have been very effective in selecting good study participants and reducing attrition from clinical trials. Those participants who seem appropriate for the trial will then be so informed and will be randomly assigned to one of the three treatment groups. Participants who do not currently have a personal care provided will be provided a list of local providers.

6. RANDOMIZATION

A study website will be used for randomization, which will include an automatic check of the completeness and success of eligibility. Fall-back methods will also be in place, which allow for randomization via phone calls if extended times without web service occur. The system provides reports of expected follow-up sequences and missed appointments, prevents withdrawing participants after randomization has occurred, and ensures concealment of the randomization scheme. To ensure blinding of the assessment staff to intervention assignment, randomization assignments will be obtained from the computerized data management system by staff who are not involved in height or weight assessments.

SNAP will adopt a simple, non-adaptive variable-block length randomization, which will ensure fairly equal allocations over time and make it difficult for staff to guess future assignments. Randomization will be stratified by clinical site to balance assignments on factors associated with each clinical site that are difficult to measure or quantify such as demography, geography, local health care personnel, local health care practices, clinical site personnel, and facilities. To ensure comparability of gender and ethnic representation across the three conditions, randomization will also be stratified by gender and ethnicity (Hispanic/Non-Hispanic white versus other race/ethnic groups). Extensive stratification is not recommended for a randomized controlled clinical trial of this size. Covariate adjustment can be used to address marked chance imbalances in measured pre-randomization characteristics.

7. RETENTION

Proactive efforts will be made to retain all participants for the entire study period including building strong rapport by sending participants birthday cards and periodic study newsletters. We will also obtain contact information (name, address, and phone number) of a family member or friend to assist in locating participants for follow-up assessments. These procedures have been used by investigators at both sites successfully with retention in recent clinical trials being 80-95% depending on point of follow-up and specific protocol.

A systematic protocol will be followed to minimize dropouts. Participants in the intervention will be called or sent an e-mail reminder before each session. If a participant has an unexcused absence, they will be contacted and helped to solve any barriers to attendance. The session materials will be e-mailed or sent to those who do not attend and make-up session will be offered. Top priority will be for assessment visits. The biggest source of dropouts in prior studies with this age group is pregnancy (15% of women in Health Hunters had a pregnancy; 11% of the women in POP). SNAP staff will stay in touch with women during pregnancy and
allow them to return to the study at 6 months post-partum, we will continue to include their weight data in our analyses except during their actual pregnancy and the 6-months post-partum.

8. INTERVENTIONS

8.1 Comparison Condition

The comparison condition (Control group) will be used to determine the rate of weight gain over 3 years for individuals who are not given an active weight gain prevention intervention. The goal is to give participants in this condition minimal intervention (so as not to alter the natural history of weight gain) but to achieve maximal retention at the annual assessments. To accomplish this, a single face-to-face group educational session will be conducted soon after randomization and participants will be presented with basic education about weight gain in young adults, including information about the types of behavior changes associated with weight gain and the health consequences of weight gain. This session will educate the Control group about the importance of self-weighing as a preventive strategy and introduce them to both the small changes and large changes approaches. The website for America on the Move and smallchanges.gov will be provided as a way to follow a “small changes” approach and several weight loss web links will be provided to illustrate a large changes approach. In addition, the Control group will be sent quarterly newsletters covering weight gain prevention topics and providing healthy recipes and exercise strategies; however, although they are provided information and education, the control will not receive the assistance in implementing these approaches that is provided in the intervention groups.

8.2 Common Components of the Active Interventions

The two interventions tested in SNAP are comparable in the frequency of contact with the interventionist, the theoretical basis (i.e., self-regulation), the basic information provided about healthy eating and physical activity, and the behavioral modification skills that participants are taught to help them make either small or big behavior changes.

8.2.1 Contact schedules

The initial intervention in both conditions consists of 8 weekly face-to-face group meetings and 2 monthly meetings (10 meetings over 16 weeks), led by interventionists with backgrounds in nutrition, exercise physiology, or behavior modification and behavioral weight control experience.

Table 8.2 Intervention Contact Schedule

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>Meetings</th>
<th>Reporting Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months 1-2</td>
<td>Weekly</td>
<td>None*</td>
</tr>
<tr>
<td>Months 3-4</td>
<td>Monthly</td>
<td>Weekly</td>
</tr>
<tr>
<td>Months 5-12</td>
<td>None</td>
<td>Monthly</td>
</tr>
<tr>
<td>Year 2</td>
<td>Annual 4 week refresher</td>
<td>Monthly</td>
</tr>
<tr>
<td>Year 3</td>
<td>Annual 4 week refresher</td>
<td>Monthly</td>
</tr>
</tbody>
</table>
SNAP is conducting the intervention face-to-face because in prior studies, lower intensity approaches (e.g., newsletters; correspondence programs) have not been effective in preventing weight gain in young adults. The only programs that have met with any success have been more intensive and involved face-to-face contact.\textsuperscript{12,13} Likewise face-to-face was more effective than Internet in preventing weight regain.\textsuperscript{9} SNAP will use a moderate intensity program with weekly meetings for the first 2 months and monthly for the second 2 months. Groups will be conducted in a closed format with approximately 20 members (i.e., the 20 participants will start and end these 10 meetings together). In subsequent years (ranging from 2–4 additional years due to the planned staggered enrollment), participants will be offered an annual 4-week refresher program. Participants will not need to stay with their original cohort for these refresher courses. Several sessions will be offered on different days and times, and participants will be able to choose the one that is most convenient for them. This concept of using open format refresher courses/campaigns was used successfully in the Diabetes Prevention Program\textsuperscript{22} and is being used currently in Look AHEAD. The proposed intervention schedule was selected with awareness of the busy lives of young adults and as appropriate for future implementation in real-world settings, such as YMCAs, employee health programs, or health clubs. In addition, make-up sessions will be offered (and attendance at these documented) and all materials will be available on the study website to help those who are unable to attend a specific session of the program.

To maintain contact with participants between meetings and to increase accountability, SNAP will supplement face-to-face meetings with use of a web-based system that participants will use to report their weight and behaviors.

8.2.2 Intervention delivery
The goal of both interventions is to prevent weight gain through the self-regulation of eating and exercise behaviors, a model that was used successfully in STOP Regain.\textsuperscript{9} All of the basic elements are used again in this weight gain prevention program. Participants will be given scales for use at home and will be taught: a) to weigh themselves daily; b) to detect small changes in weight as soon as they occur; c) to implement problem solving strategies to deal with these changes; d) to evaluate the success of these strategies; and e) to provide self-reinforcement for successful weight maintenance or to make changes in their behavior if gains occur.

To help participants detect small changes in their weight and to guide appropriate actions, they will be taught to use a red, yellow, and green weight monitoring system. Participants will use a web-based system to report their weight on the contact schedule outlined above; based on their reported weight, they will receive feedback as to their color zone for the week (see color zone descriptions below) and will be instructed to practice either reinforcing themselves or taking the corrective appropriate action. The color zones for both interventions will be identical.

**The “green zone” (Go!):** at or below their weight at the end of the 8 week intervention. Participants whose weight is in the green zone will be encouraged to reinforce themselves for their success. To teach such reinforcement, the study will initially provide small token reinforcement for participants in the green zone on a preset intermittent schedule, the equivalent
of once per month (e.g. green tea, green dollar bill, green Frisbee). These token reinforcers were very well received in Stop Regain and our pilot for this trial.

**The yellow”(Caution!) zone: weight is above the participant’s weight at the end of the program but below their starting weight.** Participants who are in the yellow zone will be warned that their weight is creeping up, with increasing intensity of the warning as they come closer to the red zone. They will be taught to return to self-monitoring of diet and activity, to identify behavior changes that may be causing the weight gain, and to use problem solving strategies to reverse these changes. Thus, behavior changes are recommended in response to any weight regain, with more urgent recommendations if weight approaches the red zone.

**The “red” (Stop!) zone: any weight at or above the participants’ starting weight.** If participants enter the red zone, more substantial changes in behavior will be prescribed (this action plan differs by treatment condition – described below). In addition, participants in the red zone at the end of the month will be asked if they would like additional help from a counselor either via phone, e-mail, or in person. Up to two individual sessions will be made available to participants during any month that they are in the red zone.

A structured protocol will be used for these individual Red counseling sessions and all contacts will be documented in the study data system. The sessions will be conducted by a nutritionist or individual experienced in behavioral weight control; the participants will speak with the same interventionist whenever possible to provide continuity of care. The contact will last about 20 minutes and have two parts—an introductory/motivational portion and a goal setting portion. The introductory portion will be based on motivational interviewing and will be similar for participants in the large and small change groups; the participant will be encouraged to reflect on their reasons for joining the study and their initial desire to prevent weight gain. Discrepancies between these initial goals and their current behavior will be discussed. The second part of the call will clearly differ by treatment group. The participant will be encouraged to consider ways in which they could stop their weight gain – using the type of techniques they have previously been taught (i.e. small or large changes, see below). For example in the Large Changes group, the participants will be encouraged to consider strategies such as returning to self-monitoring or to a calorie-controlled diet or rejoining a gym; in contrast, the Small Changes group would be encouraged to resume wearing their pedometer and to think about making an additional small change in their diet. At the end of the call, the interventionist will complete a report indicating the types of contact (phone; e-mail; in-person), the issues discussed and the participant’s plan. This contact “form” will be useful in guiding subsequent contacts (to inquire about progress toward goals set on the last call), but also will provide important process data for the trial.

**8.2.3 Modifying eating behaviors**

Both intervention groups will be taught about energy balance and how body weight relates to energy intake and expenditure. They will also learn about appropriate portion sizes and the calories in protein, fat, and carbohydrates, and will be taught basic nutrition skills such as label reading. Participants in both groups will be encouraged to consume a heart healthy diet, with a low intake of saturated fat and trans-fats and high intake of fruits, vegetables and whole grains. Prior studies have shown that weight gain in young adults is associated with increased caloric intake and percent fat; changes in dietary pattern toward a more “prudent” dietary pattern and
away from a Western pattern have also been associated with lower weight gains\(^ {24}\) and thus will be encouraged in the program.

Specific attention will be devoted to those aspects of eating behavior that have been related to weight gain in young adults, particularly fast food consumption,\(^ {25, 26}\) alcohol consumption, and sweetened beverages.\(^ {25, 27}\)

**8.2.4 Modifying physical activity**
Both interventions will also emphasize the importance of increasing physical activity and decreasing sedentary behaviors as a means of preventing weight gain. General information about the calories burned in different types of activity will be presented to both intervention groups and the importance of both programmed and lifestyle physical activity will be stressed. The program will strongly emphasize physical activity since young adults are at risk for decreasing their physical activity and changes in physical activity level and physical fitness\(^ {20, 23, 28}\) have consistently been associated with both weight gain over time and with weight regain after initial weight loss. The interventions will also seek to decrease time spent in sedentary activity since again, this has been related to weight change in young adults.\(^ {25}\)

**8.2.5 Behavior modification skills**
In addition to education about healthy eating and physical activity, participants in both groups will receive instruction in core cognitive and behavioral skills such as self-monitoring, stimulus control, problem solving, social support and assertiveness training, goal setting, and cognitive restructuring to help them implement their small or large behavior changes.\(^ {29-33}\)

**8.3. Differences Between the Two Active Interventions.**
The differences in the two active interventions are summarized in Table 8.3 and described in detail below.

**Table 8.3: Treatment Components that Differ between the Two Intervention Groups**

<table>
<thead>
<tr>
<th>Key Intervention Concepts</th>
<th>Small Changes</th>
<th>Large Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary changes recommended for maintaining weight (green zone)</td>
<td>Instructed to make one small change in diet every day</td>
<td>Start with 1200-1800 kcal/day diet to create weight loss buffer in first 8 weeks. After buffer created, gradually increase caloric intake until maintaining weight loss, but continue to consume low calorie, low fat healthy diet</td>
</tr>
<tr>
<td>Physical activity changes recommended for maintaining weight (green zone)</td>
<td>Given pedometers and instructed to increase steps by 2000 steps per day over baseline levels and maintain this level</td>
<td>Instructed to exercise for 250 min/week (50 min/day on 5 days/week) throughout the entire program.</td>
</tr>
<tr>
<td>Self-monitoring of behavior changes</td>
<td>During initial 12 weeks and refresher courses, record number of steps per day and check off whether or not a small change in diet was made every day. Self-monitor weight daily throughout the entire program.</td>
<td>Self-monitor food intake (calories and fat grams) for first 12 weeks of the program, throughout the refresher course, and if they experience weight regain. Self-monitor weight daily throughout the entire program.</td>
</tr>
<tr>
<td>What to do if regain 1 pound or more above the weight they achieve at the end of initial 8</td>
<td>Taught to resume self-monitoring of steps and small changes to diet. Use problem-solving skills, with an</td>
<td>Taught to resume self-monitoring of food intake for several days to help identify problem areas and get back on</td>
</tr>
</tbody>
</table>
The Self-Regulation Plus Small Behavior Changes Intervention will focus on making small changes in diet and physical activity on a daily basis to prevent weight gain (see Appendix 3 for sample sessions). Participants will be taught that by making one small change in how much they eat or what they eat and increasing their physical activity by 2000 steps per day, they can prevent weight gain and perhaps even lose some weight. The initial program will help participants identify and practice these small changes which they will continue to implement on a consistent, permanent basis to prevent weight gain.

**Diet:** The dietary approach used in this group is to identify small changes in what and how much participants eat each day. Although these changes are described as being approximately 100 calories, it is recognized that the calorie value of each specific dietary change will vary; rather, the general concept is that these are small, manageable changes that will produce small reductions in overall intake and can easily be made on a daily basis and maintained over time. Participants will be first introduced to the strategy of reducing the amount (portion size) of foods consumed. Specific strategies (many from America on the Move) will be suggested, including for example, leaving 3 – 4 bites of food on their plate, using only 1 slice of bread for an “open-faced sandwich”. Participants will be given a list of these strategies and asked to try one strategy each day. In subsequent weeks, participants will be introduced to small changes they can make to modify the types of food they eat; small changes when eating out and small changes in liquid calories, two areas that are particularly challenging for young adults, will also be presented. For each type of diet change, the group will brainstorm possible small changes that could be made and a list of suggestions will be provided to participants.

**Exercise:** At the start of the program, participants will be given a pedometer and asked to record their current or baseline number of steps. They will then be given the goal of increasing their daily steps by 2000 steps per day over this baseline level. The group will brainstorm ways to increase daily steps and participants will be given a handout reviewing such strategies (many of these suggestions come from America on the Move). Participants will be instructed to select a small change they can make each day in order to increase their overall steps by 2000. At the subsequent meeting, their success at implementing this behavior change strategy will be
discussed. If the participant selects a strategy that does not increase activity by 2000 steps, an additional small change will be suggested. Lifestyle changes (walking the dog; mowing the lawn) will be stressed as one way to increase exercise by 2000 steps, but the approach of adding additional minutes to structured exercise (bike riding for 10 minutes more) will be discussed at subsequent meetings.

**Self-monitoring:** Participants will be given a monthly chart to use to record their daily weight and the number of steps they take each day. In addition, they will check a box to indicate whether they made a small change in their diet during that day. The Small Changes group will complete this record of weight, steps, and whether a change in diet was made every day throughout the first 12 weeks of the program and the refresher course. These participants will be instructed to record their weight daily throughout the entire trial. If they enter the “yellow” zone, they will resume monitoring of small changes in diet and pedometer steps.

**Maintenance:** During the initial program, participants will try a variety of ways to decrease calorie intake and increase exercise. Subsequently they will be instructed to select from these strategies each day and continue to make one change in diet each day and one or more changes in activity to increase steps by 2000. If these participants experience weight gains at any time over the three years (i.e. enter the yellow zone), they will be taught to immediately return to self-monitoring of diet and exercise using their pedometer and the monthly chart to confirm that they are still making small changes in diet and achieving their step goal. They will be taught to problem solve about the causes of the weight gain. If these actions are not sufficient and weight regain continues or they enter the red zone, they will be taught to add an additional small change in both diet and activity. By making several small changes, these participants will be gradually altering their energy balance (two small activity and two small diet changes equals approximately a 400 calorie deficit which should produce almost a 1 pound/week weight loss). In addition, during the initial intervention, they will create a “toolbox” that they will be able to use if they experience weight gain. The toolbox (provided by the study) will include a compilation of small changes that can be made to decrease intake and increase activity. The toolbox will also include a new pedometer and a reminder of their prior step goal, as well as copies of self-monitoring charts. Finally, when in the red zone, participants will be encouraged to contact the program staff for additional counseling and guidance.

**Refresher courses:** At each annual refresher course, members of this group will be asked to again monitor their steps and check off whether they are making a small change in diet each day. As described above, participants who have experienced weight gains will be encouraged to increase to two small changes in eating each day and to a step level of 3000 steps over baseline. In addition, the refresher program will include a physical activity or a nutrition activity that will be fun for participants and help motivate attendance and weight control.

### 8.3.2 Self-regulation plus large behavior changes group

The focus of this intervention group will be on periodically making large changes in diet and physical activity, with the goal of losing 5-10 pounds to buffer against the weight gain that often occurs during young adulthood. Recognizing that it is challenging for young adults to pay close attention to diet and exercise at all times, this group will be encouraged to spend a few weeks each year really focusing on diet and exercise to produce a 5-10 pound weight loss, and then
throughout the rest of the year, focus on weighing themselves regularly and maintaining healthy eating habits and high physical activity levels to prevent weight regain.

**Diet:** Individuals with a BMI of 21-24.9 kg/m² will be encouraged to lose 5 pounds; those with a BMI of 25-30 kg/m² will be encouraged to lose 10 pounds. To produce these weight losses, participants in the Large Changes group will be instructed to consume either 1200-1500 or 1500-1800 calories per day, with <30% of calories from fat. The specific calorie range will be individualized for participants based on their weight and the amount of physical activity they report during baseline assessments. To stay within their recommended calorie range, participants will be taught about calorie balance and about the calorie content of different types of foods. They will be given specific meal plans modeling a low calorie low fat eating plan that they can use since this type of structure has been shown to improve weight loss. They will continue to follow the 1200-1500 or 1500-1800 calorie diet until they achieve the 5-10 pound weight loss goal, which we expect will occur for many by the end of the initial 8 week program; after reaching their weight loss goal, their calories will be gradually increased to maintain this reduced weight level and a healthy, low calorie, low fat regimen will be encouraged. The period between weeks 8 and 16 will provide an opportunity for these participants to determine the calorie level they need in order to maintain the 5 to 10 pound weight loss.

**Exercise:** The Large Changes group will be instructed to gradually increase their minutes of physical activity until achieving 250 minutes per week (5 days/week with 50 minutes per day) using activities similar in intensity to brisk walking. Since this high level of physical activity has been shown to be important for weight loss maintenance, participants in the Large Changes group will be taught to maintain this high level of activity over all subsequent years of the program.

**Self-monitoring:** During the first 12 weeks (and during each refresher course), the Large Changes group will record their weight and the specific foods they eat each day, including portion sizes, and the number of calories and fat grams in those foods and their minutes of physical activity. They will continue to record their weight throughout the trial.

**Maintenance:** After completing the initial program, the primary emphasis will be on monitoring weight on a daily basis and using the weight data to determine if and when behavior changes are needed. Individuals who start to regain weight after the initial program, but do not exceed their baseline weight (i.e. in the “yellow” zone) will be instructed to return to self-monitoring their diet and exercise and to problem solve and to identify behavior changes that may be related to their weight gain. It is anticipated that there will be variability in the weight losses achieved by participants in the Large Changes group during the initial phase of the program, and thus differences in the amount of weight the person can regain before approaching their baseline weight. Thus, persons who lose more weight initially will have created a wider “yellow” or caution zone (i.e., a wider “buffer”) for themselves. If these participants continue to regain within the yellow zone, and begin to approach the red zone, they will receive more urgent messages to take steps to get back on track. If these participants enter the red zone, they will be taught to return to the reduced calorie intake goal of 1200 to 1500 or 1500 – 1800 calories per day. They will be encouraged to use the structured meal plans and meal replacement products to achieve these goals. In addition, they will make certain that they are reaching the 250 minute
activity goal, and if needed, increase above this level. This intervention group will be provided with a toolbox of supplies to use if they experience weight gain; their tool box will include self-monitoring books, a meal plan to use for a 1200-1500 or 1500-1800 calorie diet and meal replacement products (such as Slim-Fast). If these participants enter the red zone, they will be encouraged to contact the program staff for counseling session.

Refresher Courses: The refresher courses will be 4 weeks in a row and will be used to help participants return to their 5-10 pound below baseline level. Again, a calorie and physical activity prescriptions and daily self-monitoring will be important aspects of the program. Individuals who have maintained their initial weight loss will be allowed to lose more weight if they wish, provided that they do not reduce below a BMI of 18.5 kg/m² (the lower end of the normal BMI range). The refresher classes offered to this group will include cooking demonstrations and fitness activities to provide educational and interactive ways to encourage maintenance of the 5-10 pound weight gain buffer.

9. DATA COLLECTION

9.1 Assessments
All assessments will be completed by staff members who are blinded to the participants’ intervention assignment and have been certified by the Coordinating Center in the appropriate conduct of the measures. Participants will be provided a $50 honorarium for attending each assessment session. Table 9.1 shows the schedule of assessments for SNAP.
Table 9.1 Data collection schedule

<table>
<thead>
<tr>
<th>Measure</th>
<th>Month 0</th>
<th>Month 4</th>
<th>Month 12</th>
<th>Month 24</th>
<th>Month 36</th>
<th>Month 48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthropomorphic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (primary outcome)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Height</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Behavioral and cognitive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet (Food Frequency Questionnaire)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Specific questions about diet</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Physical activity: Paffenbarger Sedentary Activity</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Objective (arm bands)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight management strategies</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Self-weighing</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eating disorders assessment</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eating Inventory</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Autonomous motivation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Smoking, alcohol use</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Medical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fasting lipids, glucose, insulin</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Medication use</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DNA, serum, plasma</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Psychological assessments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (CES-D)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Life events</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Perceived stress</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Quality of life</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><strong>Other questionnaires</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographic data</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight status of friends and family</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Treatment preference, satisfaction and post-treatment feedback</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adherence (Intervention groups only)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attendance at adherence sessions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Throughout</td>
<td></td>
</tr>
<tr>
<td>Weekly submission of weight data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Throughout</td>
<td></td>
</tr>
</tbody>
</table>

9.1.1 Anthropometric measures
- **Weight** will be measured in a hospital gown, without shoes, on calibrated scales at each assessment visit. Two measures will be completed and the average of the two will be used.
- **Height** will be determined at each assessment visit using a wall mounted stadiometer. Two measures of height will be taken and the average of the two will be used. We will repeat the measurement of height at each assessment visit because growth may still be occurring in
these young adults. The weight and height measures will be used to calculate Body Mass Index (weight in kilograms divided by height in meters squared).

- **Waist circumference** will be measured at the mid point between the highest point of the iliac crest and the lowest part of the costal margin in the mid-axillary line using a Gulik tape measure. Two measures of waist circumference will be taken; if the difference exceeds 1.0 cm, a third measure will be taken.

We have completed these measures in prior studies and will use protocols developed for Look AHEAD.

### 9.1.2 Behavioral and cognitive measures

**Diet**: Dietary intake will be assessed at baseline, month 4 and month 24 with the Block Food Frequency, a semi-quantitative food frequency questionnaire that has been used in a number of weight loss intervention trials including Look AHEAD, DPP, and PRIDE. For each food item on the Food Frequency, participants report the frequency of consumption and the portion sizes consumed. The FFQ assesses the consumption of low fat versions of 10 foods, including meats, cheeses, yogurts, and cookies/cakes and has been modified to include liquid meal replacement products and ethnic food choices. An important reason for selecting this approach to dietary assessment is that the participants can complete the FFQ on-line at their own convenience.

Data from the FFQ will be supplemented with several diet and eating behavior questions that can be asked at each assessment visit. These will include items related to frequency of meals at fast food restaurants, frequency of meals at other types of restaurants, and consumption of sweetened beverages.

**Physical Activity**. The Paffenbarger Activity Questionnaire (PAQ) will be administered as a measure of physical activity at each assessment visit. The PAQ has been used to assess leisure time activity in many weight loss trials and can be scored to provide an estimate of calories expended per week in overall leisure time activity and in activities of light (5 kcal/min), medium (7.5 kcal/min), and high (10 kcal/min) intensity. Changes in exercise on the PAQ have been shown to be predictive of weight change in overweight and obese individuals.

Given the increasing recognition of the importance of sedentary activity, independent of physical activity, we will assess sedentary activity at each assessment visit. We will use the PACE Adult Sedentary Behaviors Survey, which asks respondents to indicate the number of hours they spend on a typical weekday and a typical weekend day doing each of nine sedentary activities.

We will also include an objective assessment of physical activity at baseline, month 4 and month 24 in order to confirm the self-report data and to determine whether participants in the small and large changes conditions have different patterns of activity that reflect the different exercise recommendations given to the two groups (e.g. longer bouts of activity in the large changes condition). We will use the SenseWear Pro Armbands (Body Media, Pittsburgh PA) in this trial. The Sense-Wear Pro Armband is a newly developed commercially available device to assess energy expenditure. The device, worn on the upper arm, uses data from a variety of parameters, including heat flux, accelerometer, galvanic skin response, skin temperature, near-body temperature, and demographic characteristics to estimate energy expenditure using proprietary
equations developed by the manufacturer. The novel technology of a heat flux sensor appears to make it more accurate than prior technology in assessing expenditure. Investigators at both sites have utilized these instruments in prior studies and thus are familiar with the technology.\textsuperscript{36}

**Weight Management Strategies.** We will assess both healthy (e.g. record what you eat daily, cut out between meal snacking) and unhealthy (e.g. take diet pills, fasting) weight control practices using questions compiled from Pound of Prevention,\textsuperscript{21} NHANES and the Weight Loss Maintenance trial. Participants will be asked to indicate whether or not they used they have used each strategy within the past 6 months, and if so, to indicate how frequently they used the strategy. Participants will also indicate whether they have participated in any other commercial weight loss programs including commercial and Internet programs and/or followed any other weight loss diets (e.g. Atkins).

Frequent self-weighing is the pivotal component of self-regulation. To assess this, participants will be asked to indicate how frequently they have weighed themselves within the past 6 months, ranging from several times a day, daily, a few times a week, weekly, once a month, or less than once a month to never. Participants will also be asked to indicate the extent to which they found weighing themselves to be frustrating or motivating and how they reacted if they observed weight gains.

**Eating Disorders Assessment (EDA).** Participants will complete a questionnaire used in Look AHEAD that assesses the frequency of binge eating episodes accompanied by loss of control, and the frequency of compensatory behaviors including vomiting, diuretics, and fasting. These data will be used to identify any individuals who meet criteria for bulimia nervosa during the trial.

**Eating Inventory.** The Eating Inventory (TFEQ)\textsuperscript{37} is a 51-item self-report instrument with three factors, assessing dietary restraint, disinhibition and hunger. The Restraint factor (range 0-21) assesses the degree of conscious control one is exerting over eating behaviors. This factor has been related to successful weight loss and maintenance.\textsuperscript{38} The Disinhibition factor (range 0-16) measures susceptibility to loss of control over eating; this factor has been shown to correlate positively with frequency and severity of binge eating.\textsuperscript{39} Scores on the hunger factor range from 0-14; different diet prescriptions within weight loss interventions have been shown to influence scores on the hunger factor.

**Autonomous Motivation.** Autonomous motivation for preventing weight gain will be measured with the Treatment Self Regulation Questionnaire.\textsuperscript{40,41} Half of the items reflect autonomous motivation (e.g., “Because I feel that I want to take responsibility for my own health”) and half reflect controlled motivation (e.g., “Because I would feel guilty or ashamed of myself if I did not try to control my weight”). Participants will rate each item using a 7-point Likert scale ranging from 1 “not at all true” to 7 “very true.” We have recently reported that increases in autonomous motivation were associated with better weight loss.\textsuperscript{42} The Small Changes intervention, by focusing on self-selected changes in diet and exercise, may foster autonomous motivation for behavior change, which may in turn be associated with better weight maintenance.
Smoking and Alcohol. Questionnaires will be administered at baseline and at each assessment to assess smoking and alcohol behaviors and any changes that occur over time.

9.1.3 Clinical Measures
Blood pressure will be assessed with a Dinamap Monitor Pro 100. Cuff size will be determined by arm circumference. Two readings will be taken, with a 30-second wait between.

Fasting blood samples will be taken for analysis of lipids (total cholesterol, HDL-C, LDL-C and triglycerides) and glucose and insulin levels at baseline and month 24. In addition, we will store baseline samples of serum and plasma for later analysis for additional phenotypic markers of cardiovascular disease risk, such as inflammatory markers. These measures are collected to examine changes in specific risk factors and in the metabolic syndrome.43, 44

Medication Use. At baseline and each assessment, participants will be asked to report all prescription and non-prescription medications.

DNA will be collected to enable future studies to capitalize on a well-characterized group of young adults enrolled in a randomized, controlled trial that will allow testing of interactions between treatment group and genetic variations. By banking the DNA, SNAP will have the maximum flexibility to select a genetic study design and potential candidate genes that reflect the state of the art as the trial is completed.

9.1.4 Psychological assessments
Depression. The Center for Epidemiologic Studies Depression Scale (CES-D)45 is a self-report depression scale designed to measure depression symptoms in the general population. The self-test measure includes 20 items that relate to depressive feelings and behaviors during the past week. The CES-D will be administered at baseline and to determine whether the interventions are associated with improvements or worsening in mood relative to the control.

Life Events. The life events questionnaire from the CARDIA study lists 67 events and participants are asked to indicate whether or not that event has occurred in the past year. We have chosen to use the CARDIA life events questionnaire in preference to other similar questionnaires (e.g. Holmes and Rahe)46 because it was developed specifically for young adults and reflects the type of life events that occur most commonly in this age group.

Perceived Stress. The Cohen Perceived Stress Scale47 is a 4-item self-report instrument that captures the participant’s perception of stress in their lives over the past month. The Perceived Stress Scale poses general questions about current stress levels. All items begin with the phrase: In the past month, how often have you felt…? This instrument has been used in many studies and has excellent reliability and validity.47,48

Quality of Life. All participants will complete the CDC Health-Related Quality of Life measure (commonly referred to as “Healthy Days Measures”) at each assessment. This 4 item questionnaire has been utilized in the BRFSS and NHANES and has been shown to have appropriate reliability, validity, and responsiveness to change.
9.1.5 Other measures
Basic demographic information will be collected, including age, race/ethnicity, occupation; education and prior experience in weight loss programs.

Weight status of friends and family. Based on the increasing recognition of the importance of social networks, we will ask participants to indicate the weight status of their friends and family members. This information will be collected at each assessment visit to determine if changes in weight in the participant are related to the weight status of others in their social network.

Treatment Preference and Satisfaction. Prior to randomization, each participants’ preference for each of the three arms of the trial will be recorded to determine whether initial preference for small or large changes group relates to outcome in participants assigned to their preferred or non-preferred alternative. Participants will also complete a post-treatment process evaluation. This information will provide a more complete picture of how SNAP interventions are perceived and experienced by young adults and may provide valuable information about how to modify the programs for future use in this population.

9.1.6 Measures of adherence
Data will be collected on the number of intervention visits attended in the two active intervention groups. Attendance at treatment sessions is anticipated to decline over time, but in keeping with prior studies in the weight control literature, those who attend more sessions are expected to have better weight loss outcomes. Data will also be collected on any individual make-up sessions attended and individual “red-zone” counseling sessions.

Participants in the intervention groups will be instructed to report their weight weekly via the study website. These data will be tabulated to derive a measure of percent of weeks in which weight was reported. In STOP Regain, attendance and weight reporting were significantly correlated with each other, and weight reporting was associated with successful maintenance of weight loss.

10. DATA MANAGEMENT and QUALITY CONTROL

10.1 Data Management
The SNAP web-based data entry system allows for direct data entry by participants and entry by staff from data collected on paper forms. Data entered into the system are immediately available for review and reporting. Participants will have the option to enter select forms directly into the website prior to their clinic visit.

10.2 Monitoring Data Quality
On-line reports will be used to provide up-to-the-minute access to data. Regular reports will also be sent to the Steering Committee, and a subset of these will be continually updated on the study website. These will allow the study to verify completeness, timeliness, reliability, and accuracy of collection and coding of its data. The quality reports include comprehensive data on all quality control activities, including protocol adherence and violation, training, retraining and
certification, site visit reporting, random repeat lab measures, and data from monitoring the
distribution of individual values and of mean or median values by Clinical Site. Included will be
comparisons of measures of distribution of values over time and between Clinical Sites. The
Coordinating Center will develop and maintain standards to identify outlying values, and initiate
and coordinate separate review of these observations for accuracy.

10.3 Website and Security

The SNAP website is the foundation of its coordination, communication, management, data
text and transmission, quality control, and distribution of information. Data in central
Coordinating Center databases will be kept secure.

Care in handling participant identifying information and secure data transfer are essential to
SQG. Any data transferred outside the Coordinating Center is done securely. Secure internet
transfers (secure FTP or encrypted webpage downloads) within the study will contain only the
necessary identifying data.

10.4 Quality Control

Quality assurance and quality control is a shared responsibility among the SNAP team of
investigators. The validity and eventual acceptability of study results depend in part on
maintaining data integrity, documenting dropouts, monitoring and assessing protocol adherence,
and unbiased measurements. The quality control program includes reviews of questionnaires,
and duplicate measurements for instrument based work (e.g., anthropometry, blood pressure).
The goal of all quality control work is to maintain a high degree of data quality throughout the
course of the study and to document study quality for publications.

Of the many possible sources of heterogeneity between Clinical Sites, one of the largest and
most controllable is uniformity in the application of the protocol. Central training, staff
certification and site visits will be used to enhance standardization across the Clinical Sites.

A detailed and complete Manual of Operations is necessary for a successful study. The Manual
of Operations serves as the study-wide procedural handbook and contains detailed information
describing every aspect of the study including thorough descriptions of procedures for
recruitment, clinical and lab measurements, data collection and handling, monitoring and follow-
up.

The web-based system will be used to generate and resolve data queries. It provides an
immediate correction to the database, creates a reliable audit trail, and minimizes duplicate
requests for data cleaning to the clinics. Clinical Sites will receive regular reports on missing
and incomplete forms, and results of quality assurance checks.

Secure web-based file uploads that include basic data checks are used for quality assurance for
Central Laboratory data. Further checking occurs when uploaded files are converted into SQL
databases. The Coordinating Center will maintain logs of data received from all sources, and
pursue missing data and correctable errors.
Standardized procedures for measuring cardiovascular disease risk factors are an important part of the quality process. The Quality Control Committee will define local blood collection and processing requirements, developing training and certification procedures for Clinical Site staff.

11. PARTICIPANT MANAGEMENT AND SAFETY
11.1. Introduction
The following sections define adverse events, serious adverse events, and unanticipated events and the procedures that will be followed in the trial to reduce the risk of all such occurrences.

11.2. Definitions
Definitions are obtained from the “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events Office for Human Research Protections (OHRP)” [http://www.hhs.gov/ohrp/policy/AdvEvntGuid.htm]. The requirements and processes of the National Heart, Lung, and Blood Institute are also implemented.

11.2.1. Adverse events and serious adverse events
An adverse event is defined as any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. Abnormal laboratory results will be considered adverse events if they are not refuted by a repeat test conducted to confirm the abnormality or if the abnormality is of a degree that requires active clinical management.

Adverse events will be collected and reported from the beginning of study-related procedures to the end of the study follow-up period for an individual participant. At each assessment visit, SNAP staff will specifically query participants for adverse events using the event form (see Appendix 4). Information on adverse events may also be reported to study staff during intervention contacts, as well as through telephone calls and emails. All adverse events will be recorded on the study interim event form. Adverse events will be followed until resolution, stabilization, or until it is determined that the study participation is not the cause.

Consistent with NHLBI guidelines and OHRP policy, serious adverse events (SAEs) are adverse events that meet any of the following criteria: fatal or life-threatening, result in significant or persistent disability, require or prolong hospitalization, result in a congenital anomaly/birth defect, or are important medical events that investigators judge to represent significant hazards or harm to research subjects. Any adverse event that meets any of these criteria (e.g. results in hospitalization) will be documented and reported as a serious adverse event.

11.2.2. Unanticipated problems
An unanticipated problem (UP) is defined as any incident, experience, or outcome that meets all of the following criteria: 1) unexpected 2) related or possibly related to participation in the research; and 3) suggests that the research places subjects or others at a greater risk of harm than
was previously known or recognized. According to OHRP regulations, an incident, experience, or outcome that meets the three criteria for an UP generally will warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others. Only a small subset of adverse events will be unanticipated problems.

11.3. Reporting of Serious Adverse Events and Unanticipated Problems

Selected serious adverse events will be reported to the Coordinating Center within 24 hours of knowledge of the event; these will include any deaths and serious adverse events that occurred on-site. The Coordinating Center will be responsible for timely reporting to the NIH, the DSMB, and other pertinent regulatory authorities. The Coordinating Center will provide reports of serious adverse events for review by the DSMB at their meetings.

If an adverse event that meets criteria for an unanticipated problem occurs at a SNAP cite, the Principal Investigator of that site will promptly report the problem to their institution’s IRB, as required by OHRP and NHLBI policy. Any event/problem that is unexpected, and possibly related to study participation, whether fatal, life threatening, or serious (serious adverse event or unanticipated problem) will be reported to NHLBI within 7 calendar days. An unanticipated problem suggesting greater risk of harm than previously known or recognized will be reported within 30 calendar days to the project office at NHLBI.

11.4. Potential Risks to Study Participants

11.4.1. Potential risks/adverse events due to study participation

SNAP presents low risk to study participants, given the young age of the study population and the nature of the interventions and study measurements. Participants may experience faintness or bruising from the collection of the blood sample, while infection at the site is possible but rare. Increasing physical activity may result in joint discomfort, muscle soreness, exacerbation of pre-existing hernia or musculoskeletal injuries, exacerbation of exercise-induced asthma, and new-onset minor injuries including sprains and fractures. Participants may not lose weight or may gain weight. Cholecystitis may occur with weight loss. Transient increases in the risk of sudden death and acute myocardial infarction occurring during a bout of vigorous exercise have been observed, especially in previously sedentary individuals, but these events are expected to be rare in young adults of the age range included. Adverse events that may occur with weight loss and increased physical activity, including fractures, sprains, acute asthma exacerbation requiring emergency care, and gall bladder problems will be carefully monitored and reported.

Given the age and weight range of this population, the greatest concerns are that participants may engage in unsafe dietary practices, lose weight more quickly or to lower levels than recommended, or develop untoward psychological reactions. Previous studies by Stice and colleagues\textsuperscript{50, 51} have shown that normal weight women, aged 18-29, who were placed on calorie restricted diets for 6 weeks and lost significant amounts of weight, had decreases in bulimic symptoms relative to controls. Other weight gain prevention studies also indicate that participants in these programs increase their use of healthy weight control practices and decrease their use of unhealthy practices.
11.4.2 Anticipated adverse events in young adults
Adverse events, particularly serious events, not related to study participation are expected to be
uncommon in this study of lifestyle intervention in generally health young adults. Nevertheless,
young adults in this age range do experience acute health conditions and physical trauma that
could result in serious adverse events, including disability, hospitalization and even death.
Common causes of serious adverse events and/or hospitalization in this age range include mental
disorders, digestive system diseases, unintentional injuries, genitourinary diseases, respiratory
diseases, musculoskeletal diseases, endocrine diseases, neoplasms/cancer, diseases of the heart,
pregnancy and pregnancy-related complications, and infections. Births with congenital
anomalies also occur although rates are rare. Other adverse events that occur in young adults
include the development or worsening of eating disorders (e.g. bulimia nervosa), spontaneous
and elective abortion, asthma exacerbation, and various injuries. The most common causes of
death in this age range in the US are unintentional injuries (accidents, homicide), intentional
injury (suicide), malignant neoplasms, diseases of the heart, congenital malformations, HIV
disease, pregnancy/childbirth/puerperium, cerebrovascular diseases, diabetes mellitus,
influenza/pneumonia, chronic lower respiratory diseases, chronic liver disease, and septicemia.

11.4.3. Minimization of risks
The SNAP protocol and interventions are designed to minimize the occurrence of any untoward
effects. During the screening process, potential volunteers will be evaluated to determine
whether it is safe for them to participate in the planned intervention. Medical problems that
increase risk of study participation are assessed through questionnaires and telephone interviews,
prior to randomization. The goal of these assessments is to detect conditions by history, such as
recent major surgery, symptomatic conditions such as weight bearing pain, and asymptomatic
conditions, such as eating disorders. To ensure medical readiness to begin physical activity,
subjects will complete a physical activity readiness questionnaire (PAR-Q). The PAR-Q
assesses for the following medical conditions: heart problems, chest pains, faintness or dizzy
spells, high blood pressure, bone or joint problems such as arthritis that has been or could be
aggravated by exercise, prescription medication use, and other medical reasons why exercise
would not be advisable. Participants endorsing items 1-3 on the PAR-Q (experience of heart
problems, frequent chest pains, or faintness or dizziness) will be excluded from the study.
Participants endorsing other items (e.g., 4-7) will be required to obtain physician’s consent to
participate. This screening protocol has been used successfully in our prior studies and 44% of
overweight and obese participants required physician consent to participate. We anticipate lower
rates in this trial due to recruitment of younger and primarily normal weight or moderate
overweight individuals who likely have fewer comorbid conditions and medical usage.

All participants will be advised about safe weight loss or maintenance practices including dietary
change and increasing physical activity at the initial group meeting. Participants will be advised
to gradually increase their physical activity and to use walking as a primary form of activity and
will be taught that the appropriate rate of weight loss is 1 to 2 pounds per week. In addition, we
will carefully monitor changes in weight during our trial. We will collect information at each
assessment visit on hospitalizations for any psychiatric problem, including depression and eating
disorders, and provide these data to the DSMB. We will track weight changes (using assessment
data for controls and all weight data for intervention participants) and identify any individual
who loses more than 20% of their body weight, who loses weight at a rate exceeding 2 pounds per week during the intervals between the planned clinic assessments, or who has a BMI of 18.5 kg/m² or below at any point during the program. We will meet individually with these participants within 2 weeks, discuss our concerns with them, and make appropriate referrals. We will also arrange to see these participants again 1 month later. If there is no improvement in weight status, the participant will be unable to continue to participate in the interventions.

Blood pressure will be measured at each clinic visit. We will use the JNC guidelines and inform any participant with Stage 1 hypertension (blood pressures of 140-159/90-99 mmHg) to be evaluated by their physician within 1 month; those with Stage 2 hypertension (blood pressures of 160-179/100-109 mmHg) to be evaluated by their physician with 2 months. If blood pressures >180/110 mmHg, participants will be recommended to see their physician within 1 week or evaluated immediately depending on clinical situation and complications, based on a review conducted by a study clinician. All information about blood pressure levels will be conveyed to participants verbally at the time of the blood pressure measurement and in writing immediately after the visit with the above recommendations regarding contacting their physician. We will caution participants with elevated blood pressures about doing physical activity until they are able to have their blood pressures re-checked. Fasting glucose and lipid values will be obtained only at baseline, month 4 and month 24. The results of these tests will be available within about 2 weeks of completing the blood work and will be conveyed to participants in written format. If LDL-cholesterol levels exceed 160 mg/dl or triglycerides exceed 500 mg/dl, participants will be asked to contact their physician. If glucose levels are <60 or >126 mg/dl, participants will be informed of these values and given the option of having them repeated at our clinic or seeing their physician.

We will also monitor any major musculoskeletal problems that develop during the intervention (e.g. broken bones) and determine whether these appear related to our intervention. Participants who develop musculoskeletal problems or other health problems that may affect the safety of the intervention will be instructed to stop exercising until the problem resolves and their physician approves resumption of physical activity.

Since young adults are targeted in this trial, we expect that pregnancies will occur. We will stop all intervention activities during the pregnancy. However, at 6 months post-partum, we will encourage participants to return to the intervention and the assessments for this trial.

All participants will be given an identification code to enter weight information on the phone or internet thus protecting confidentiality.

All key personnel will have attended the required courses on human subject protection and HIPAA regulations, and certificates of IRB completion are on file with the Miriam Hospital, the University of North Carolina, and Wake Forest University Health Sciences. Subjects will be recruited through newspaper advertisements, community organizations, worksites, and postings to Internet sites. Participants who are eligible based on initial telephone screening will be invited to attend an orientation session during which all aspects of this study will be described in detail and individuals will be given an opportunity to ask specific questions of the investigators regarding this study. Following this orientation session, individuals expressing a desire to
participate in this will be asked to sign an Informed Consent Form which has been approved by the Institutional Review Boards at the Miriam Hospital and the University of North Carolina, and Wake Forest University Health Sciences. In addition we will comply with all HIPPA regulations.

12. INTERIM ANALYSES AND MONITORING

Regular progress reports will be provided to the Data and Safety Monitoring Board (DSMB). These will describe recruitment, adherence, conduct, safety, study measures and outcomes.

We do not propose to conduct formal interim statistical tests on efficacy. Our reasoning for this is that this trial is not masked, the proposed interventions are based on publicly available research, and there is not a strong ethical imperative to terminate one or more arms before the planned end of the trial on the basis of efficacy. Even if differences between arms occur early, continued study of all three arms allows for better assessment of long-term effects and perhaps a greater chance to detect differences between the active intervention arms.

We also do not see a strong rationale to develop specific rules for stopping the trial early for futility. The time courses of intervention effects, in relation to the Control group, may be difficult to project from interim data. We are prepared, if requested by the DSMB at any point, to calculate interim statistical power for its review. Projections of interim power can be made under several scenarios for future data, including assumptions that current trends continue or that the future data reflect the relative effects used in the design of the trial.

Safety reports will tally adverse events by intervention assignment and postulated relationship to the trial interventions; event rates will be reported per person year of follow-up.

The DSMB will consider, midway through the trial, whether there exists a strong rationale for developing a proposal to provide for post-trial follow-up of participants. If so, a plan for early unmasking of the clinical center Principal Investigators will be developed to enable the preparation of this proposal. It will be necessary to reconsent participants for any extensions of planned follow-up.

13. ANALYSIS PLANS

For the primary analysis, SNAP will analyze participants according to their randomization assignment and include evaluable data from all visits. Supporting analyses will examine relationships between markers of intervention adherence and outcomes. Inferences will be 2-tailed. Our primary analyses will include only clinic site as a covariate. The impact of any chance imbalances in baseline characteristics in the participants randomly assigned to the three intervention conditions will be explored. Secondary analyses will assess the impact of any marked imbalances using covariate-adjustments.

13.1 Primary Hypotheses
The primary outcome measure, changes in weight from baseline over time, will be assessed at 4-, 12-, 24-, 36- (80% of cohort), and 48-months (20% of cohort). It will be contrasted among intervention groups using generalized linear models fitted by maximum likelihood with an unstructured covariance matrix. Estimated mean differences for each pairwise comparison will be developed using linear contrasts and assessed with Wald statistics, using Bonferroni adjustment to control total Type I error to be 0.05 across the three comparisons. In the primary analysis, missing weight measurements will be assumed missing at random, however the following supporting analyses will be conducted. Differences in baseline characteristics between participants with complete versus incomplete follow-up will be described. To gauge the sensitivity of our results to any changes in height, we will conduct supporting analyses of changes in BMI.

13.2 Secondary Hypotheses

To address secondary aim 2, pairwise differences in the secondary outcome measure, weight gain (yes/no), will be assessed using generalized estimating equation (GEE) methods, which control for the intra-subject correlations in this dichotomous measure over time. The three pairwise comparisons will be tested with the significance level equally distributed to control the overall Type I error to be 0.05. Wald statistics will be used to test the relative difference in the parameter \( \beta_i \) between intervention assignments in the model: \( \text{Logit}(p_{gijk}) = \beta_0 + \beta_C C + \beta_I I + \beta_T T + P \) where \( C \) denotes the covariates (clinical centers identified by “g”), \( I \) is a marker for the intervention “i”, \( T \) is a maker for time (i.e. the visit “j”) and \( P \) is marker for individual participant “k”. In separate supporting analyses, in addition, Markov models will be fitted to parameterize the transition rates among the three states of no weight gain, weight gain, and missing data. Pairwise differences in changes of behavioral and psychosocial measures will be made using generalized linear models and GEE, as above.

Secondary aim 3 is an assessment of pairwise differences among intervention arms at 24-months post-randomization. This will be done using linear constrasts and Wald tests to define and test differences at this time point within the framework of the general linear models used in aim 1. Two-sided tests will be used with Bonferroni-adjustment to maintain overall Type I error for this secondary aim at 0.05.

Generalized linear models will be used for aim 4, in a manner similar to that used for assessing weight changes. The effects on outcomes of demographic and psychological measures will be examined (aim 5) by including initial BMI, ethnicity, age, scores on the eating inventory, and intervention preference. Significant interaction effects will be plotted to illustrate the moderating effects, further assisting the interpretation for whom and under what circumstances the intervention has different effects. The active interventions tested for this trial aims to produce changes in diet, physical activity, restraint, and self-regulatory behaviors. Secondary aim 6 examines potential mediators of the effect of intervention, i.e., whether or not changes in diet, physical activity, restraint, and self-regulatory behaviors are in the causal pathway between the intervention and outcomes. For the primary outcome of weight gain, a continuous measure, a series of three linear regression models will be fit to test for mediators following the procedures introduced by Baron and Kenny. The Sobel’s test will be used to test the significance of the indirect effect. The joint effects of multiple mediators will also be tested. For the secondary
outcome of weight gain (yes/no), we will run logistic regression models to assess mediational effects.54

Supporting analyses will be used to explore other ways to summarize the longitudinal dichotomous outcome of weight gain by using survival analyses to explore the distribution of times until the first weight gain and Poisson regression to model the proportion of examination times when weight gain was observed.

We pre-specify three planned subgroup comparisons. We will assess, using tests of interaction, whether the relative efficacy of the intervention varies according to baseline BMI (<25 kg/m² versus ≥25 kg/m²), age (<25 years versus ≥25 years), and gender.

13.3 Supporting Analyses

The fidelity of intervention delivery within the two Clinical Sites will be assessed by comparing measures of adherence and weight control. Adverse events will be tallied by intervention assignment and for important clinical subgroups.

14. DATA DISTRIBUTION AND SHARING

Participant consent will specifically allow data sharing among SNAP sites including the Coordinating Center and investigators and subsequent distribution of de-identified data. Study databases will be distributed to clinical site principal investigators after the trial’s end to facilitate continued data exploration.

NIH policy (issued 2003) states: “We believe that data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health. The NIH expects and supports the timely release and sharing of final research data from NIH-supported studies for use by other researchers.” SNAP data will be owned jointly by the individual clinical centers, NIH, and the coordinating center. The SNAP investigators will make no use of study data, nor disclose them to any other parties, except as specified in the Protocol or Manual of Operations or approved by the study group. The Coordinating Center will provide edited relevant data to approved ancillary study principal investigators. Only data approved by the study group will be released. The timing of data release must also be approved by the study group.

If ancillary studies are added to SNAP, their principal investigators will be responsible for providing the coordinating center edited ancillary study-specific data within 1 year of their termination. Ownership of such data is shared by the ancillary study Principal Investigator and the Coordinating Center. When the Coordinating Center ceases to function as an analytic resource to SNAP, it will release a fully documented copy of all data to each Clinical Site and the NIH. Decisions regarding disclosure of data to other parties, such as pharmaceutical companies or the FDA, shall be determined by the study group. Confidentiality of individual participants will be maintained with all releases of data.”
Within two years of when data collection ends, the final SNAP study analytical database will be processed according to HIPAA rules for public data sharing. We will de-identify participant data, using standard processes that include removal of identifiers, translation of dates and ages to delta time values, and assignment of random study identifiers. This will yield a series of de-identified data files, which will be available in a standard formats that are readable across a variety of applications and operating systems. The following documentation will be provided: data dictionary, data code book, valid variable ranges, protocol, procedure and operational manuals, and electronic versions of forms. Data sharing files and documentation will be provided by the Principal Investigator through an industry acceptable medium. Any stored laboratory samples, including DNA, will be transferred to the NIH repository two years after the end of the study.

The SNAP website will serve as a central distribution point for publicly available content. The site will contain recruitment materials and study brochures, community education materials, links to online materials, and contact information. Content management tools can be used to make as much of the content database driven as possible in order to facilitate support. File upload systems will allow approved staff to manipulate website content and allow regular review and updates.

15. TIMELINE

The timeline for SNAP consists of three phases: start-up, recruitment/follow-up, and analysis/close-out. The sample size and power estimates for this trial that were presented above are based on the expectation that Cohort 1 (N = 120) will have 48 months of data, Cohorts 2, 3 and 4 will have 36 months of data and Cohort 5 will have 24 months of data. Given these goals, recruitment will need to proceed as follows: Cohort 1 must be recruited by May 2010; Cohort 2 must be recruited by January 2011; Cohort 3 must be recruited by April 2011; Cohort 4 must be recruited by May 2011; and Cohort 5 must be recruited by January 2012. Figure 1 presents a proposed timeline for the recruitment/follow-up phase that satisfies these goals.

16. ORGANIZATION

The relatively small size and the experience of its investigators allow SNAP to operate with a streamlined organization and few committees. The Steering Committee will be the primary governing body for the study, with each Principal Investigator accorded one vote. The Intervention Committee will oversee the design and implementation of the interventions. The Quality Control Committee will oversee the design and implementation of the data collection system. A Data Safety Monitoring Board (DSMB) will be convened by NHLBI and will be responsible for overseeing the safety and conduct of this trial.
Figure 1. Proposed timeline for recruitment/follow-up

<table>
<thead>
<tr>
<th>Month</th>
<th>Year</th>
<th>Study Month</th>
<th>Wave 1</th>
<th>Wave 2</th>
<th>Wave 3</th>
<th>Wave 4</th>
<th>Wave 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sept – Oct</td>
<td>2009</td>
<td>01-02</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov – Dec</td>
<td>2009</td>
<td>03-04</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Feb</td>
<td>2010</td>
<td>05-06</td>
<td></td>
<td></td>
<td>N = 120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar – Apr</td>
<td>2010</td>
<td>07-08</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>May – June</td>
<td>2010</td>
<td>09-10</td>
<td>Base</td>
<td></td>
<td>N = 120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>July – Aug</td>
<td>2010</td>
<td>11-12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sept – Oct</td>
<td>2010</td>
<td>13-14</td>
<td>4</td>
<td></td>
<td>N = 120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov – Dec</td>
<td>2010</td>
<td>15-16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Feb</td>
<td>2011</td>
<td>17-18</td>
<td>Base</td>
<td></td>
<td>N = 120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar – Apr</td>
<td>2011</td>
<td>19-20</td>
<td></td>
<td></td>
<td>Base</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May – June</td>
<td>2011</td>
<td>21-22</td>
<td>12</td>
<td>4</td>
<td>Base</td>
<td>N = 120</td>
<td></td>
</tr>
<tr>
<td>July – Aug</td>
<td>2011</td>
<td>23-24</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sept – Oct</td>
<td>2011</td>
<td>25-26</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov – Dec</td>
<td>2011</td>
<td>27-28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Feb</td>
<td>2012</td>
<td>29-30</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar – Apr</td>
<td>2012</td>
<td>31-32</td>
<td></td>
<td>12</td>
<td>Base</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May – June</td>
<td>2012</td>
<td>33-34</td>
<td>24</td>
<td></td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>July – Aug</td>
<td>2012</td>
<td>35-36</td>
<td></td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sept – Oct</td>
<td>2012</td>
<td>37-38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov – Dec</td>
<td>2012</td>
<td>39-40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Feb</td>
<td>2013</td>
<td>41-42</td>
<td></td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar – Apr</td>
<td>2013</td>
<td>43-44</td>
<td></td>
<td>24</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May – June</td>
<td>2013</td>
<td>45-46</td>
<td>36</td>
<td></td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>July – Aug</td>
<td>2013</td>
<td>47-48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sept – Oct</td>
<td>2013</td>
<td>49-50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov – Dec</td>
<td>2013</td>
<td>51-52</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Feb</td>
<td>2014</td>
<td>53-54</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar – Apr</td>
<td>2014</td>
<td>55-56</td>
<td></td>
<td>36</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May – June</td>
<td>2014</td>
<td>57-58</td>
<td>48</td>
<td></td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>July – Aug</td>
<td>2014</td>
<td>59-60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
16. BIBLIOGRAPHY


42. Gorin A, Pinto A, Smith-West D, Niemeier HM, Fava JL, Wing RR. Losing weight because you want to rather than because you feel you have to: Motivational predictors of weight loss outcomes. Paper presented at: The Obesity Society 2007 Annual Scientific Meeting, 2008; Phoenix, AZ.


1. EXECUTIVE SUMMARY

Young adults, aged 20-35 years, experience the greatest rate of weight gain, averaging 1-2 lbs/yr. Over time, this weight gain is associated with a worsening in cardiovascular disease risk factors and an increase in the prevalence of metabolic syndrome. Given the difficulties in producing sustained weight loss later in life, preventing weight gain from occurring during this critical period is key to curbing the obesity epidemic. The Study of Novel Approaches for Prevention (SNAP) is a 2-center randomized trial designed to test whether behavioral interventions based on self-regulation can prevent weight gain in young adults (18-35 years; body mass index (BMI) 21-30 kg/m²). Approximately 600 participants will be recruited over two years and randomly assigned to a control condition (N=200), self-regulation with small changes (N=200) or self-regulation with large changes (N=200). The Small Changes group will be taught to make small, consistent, changes in eating and exercise behavior to prevent weight gain or reverse weight gain if it occurs whereas the Large Changes group will emphasize periodic, larger changes in eating and exercise, with a goal of producing weight loss and thereby providing a buffer against anticipated weight gain. The primary aim of the trial is to test whether the magnitude of weight gain from baseline across an average planned follow-up of three years differs across the three groups, with a priori hypotheses that weight gain will be greater in the Control group than in either intervention and greater in the Small Changes than Large Changes group. Secondary aims are to compare the three groups on a) the proportion of participants in the three groups who gain less than 1 pound over the planned follow-up, b) the mean difference in weight gain from baseline to 24-month follow-up, c) the changes in behaviors and psychosocial measures (diet, physical activity, dietary restraint, frequency of self-weighing, depression, and occurrence of abnormal eating behaviors), and d) the changes in cardiovascular disease risk factors (blood pressure, lipids, insulin sensitivity, and waist circumference). The trial will also examine the association among changes in behaviors, weight, and cardiovascular disease risk factors and examine variables that may moderate the effects of the intervention (including gender, ethnicity, initial BMI, age) and potential mediators of the effects of the intervention (including changes in diet, activity, and self-regulatory behaviors). SNAP is member of the Early Adult Reduction in Weight Through Lifestyle Interventions (EARLY) consortium of clinical trials funded by the National Heart, Lung, and Blood Institute.

2. BACKGROUND

Recent studies have shown that individuals who have favorable cardiovascular risk profiles as young adults have very low long-term risk of cardiovascular disease and longer survival. In a study of over 7300 women, only 20% had a favorable cardiovascular disease risk profile at age 18-30 (including BMI <25 kg/m², normal blood pressure, normal lipid levels, not smoking and no diabetes). However, in this 20%, coronary heart disease and cardiovascular disease were very rare. Over a 31-year follow-up, the multivariate adjusted cardiovascular disease mortality hazard ratio for low risk women was 0.19 compared with women with two or more high risk factors.
Other studies\textsuperscript{5,6} have confirmed the benefits of having optimal levels of cardiovascular disease risk factors at young and middle age, and shown that those with optimal risk profiles report better quality of life, lower medication use and prevalence of clinical diseases, and lower average annual health care costs in older age.\textsuperscript{7,8} These findings emphasize the need to prevent the development of adverse risk factors in young adults.

A key factor associated with the worsening in cardiovascular disease risk factors in young adults is weight gain. The Coronary Artery Risk Development in Young Adults (CARDIA) Study,\textsuperscript{2} which followed over 3,300 black and white men and women, showed that young adults have an average weight gain of 15 kg over 15 years. Only 16.3\% maintained a stable BMI over the 15 years, but individuals who remained weight stable had essentially unchanged levels of all of the components of the metabolic syndrome, regardless of their initial body mass index, age, race, or gender. In contrast, those who gained weight had worsening in cardiovascular risk factors and increased prevalence of the metabolic syndrome. These studies suggest that an important public health approach to preventing heart disease in later life would be to prevent weight gain, and the associated worsening in risk factors, during young adulthood.

Targeting young adults for weight gain prevention is important not only to prevent the increase in cardiovascular disease risk factors in the young adults themselves, but because it may also reduce the risk of obesity among offspring. Parent obesity level is among the strongest independent predictor of weight status in children. With the average maternal age of first childbirth in the U.S. at 25 years, preventing weight gain during this high-risk period and beyond may have a positive ripple effect on childhood obesity as well.

To date, there has been no intervention that has been shown in a rigorously conducted randomized controlled clinical trial to be successful in preventing long-term weight gain in young adults. SNAP will test two interventions for use in young adults. These interventions will both be based on the theory and principles of self-regulation. Self-regulation was the core of STOP Regain, our weight loss maintenance program that prevented weight regain over an 18-month period.\textsuperscript{9} In STOP Regain, participants were asked to weigh themselves daily, compare their weight to a goal weight (weight at the start of the program), and then depending on the correspondence between the two, either making adjustments in eating and exercise behaviors or provide self-reinforcement. In addition, since there is little external reinforcement for maintenance of body weight, we also included a system for reporting weights, thereby increasing accountability, and periodic reinforcement for continued weight loss maintenance. The importance of frequent self-weighing, the cornerstone of self-regulation, has also been supported in secondary analyses of an existing prevention program. In a reanalysis of data from the Pound of Prevention study, Linde et al.\textsuperscript{10} reported that those individuals who reported weighing themselves daily lost weight over 1 or 2 years follow-up, whereas those who weighed less frequently than daily experienced weight gains. Importantly, only 9\% of young adults enrolling in a weight gain prevention intervention report weighing daily at baseline. Given that so few young adults weigh themselves daily, we believe that extending our successful work on self-regulation to this age group is a critical aspect of weight gain prevention during this high-risk period.
Two different self-regulation interventions for weight gain prevention will be compared in this trial—one intervention will focus on making small, consistent changes in eating and exercise behavior to prevent weight gain or reverse weight gain if it occurs, whereas the other will emphasize larger changes in eating and exercise that occur periodically, with a goal of producing weight loss and thereby providing a buffer against anticipated weight gains. Evidence for the small changes approach comes from the theoretical papers and empirical studies of Hill and colleagues, suggesting that increases in activity of 100 kcal per day and decreases in intake of 100 kcal per day should be sufficient to prevent weight gains of 1 to 2 pounds per year. Behavioral theory also suggests that such small changes (i.e., gradual shaping of new behaviors with small incremental changes toward a goal) should be easier to initiate and maintain than larger behavior changes since they represent less drastic modifications in behavior. SNAP will target the behaviors that appear most problematic for this age group, including soda and fast food consumption and sedentary activities.

The other approach will focus on periodic prescription of larger behavior changes designed to produce weight loss. This approach was shown to be effective in the Women’s Healthy Lifestyle Project (WHLP), a study of women during the menopause that actually succeeded in preventing weight gain and the worsening in cardiovascular disease risk factors over a period of 5 years. Women in the intervention group of WHLP participated in an initial behavioral intervention designed to produce a 5-15 pound weight loss as a means of counteracting the weight gains expected with aging. The intervention group lost an average of 0.2 lbs over the 5-year intervention whereas the assessment only group gained 5 pounds on average. The intervention group also had significantly smaller increases in LDL-cholesterol, triglycerides, glucose and waist circumference. Theoretically these larger behavior changes should be easier to implement because they yield greater immediate reinforcement from the resulting weight loss and in addition provide an opportunity for participants to practice the skills they might need to use if they experience weight gains in the future. Prior research by Tate and Wing indicate their ability to produce weight loss in young adults (average of 7 pounds in a 6 month Internet weight loss program and 14.7 pounds after 6 months in a face-to-face program), supporting the feasibility of this approach as a weight gain prevention strategy in young adults.

Although there is evidence supporting the use of a self-regulation model and suggesting potential benefits to small and large behavior change approaches, this study will be the first trial to compare these interventions and evaluate their efficacy, relative to a control condition, in the prevention of weight gain in young adults.

3. OVERVIEW OF TRIAL DESIGN
3.1 Trial Design
SNAP is a 3-armed randomized controlled clinical trial, comparing a self-regulation plus small behavior changes intervention, a self-regulation plus large behavior changes intervention, and a control condition (referred to as “self-guided behavior changes”) on magnitude of weight gain over an average follow-up of 3 yrs. The trial targets enrolling 600 adults (300 at Miriam Hospital and 300 at the Univ. of North Carolina), aged 18-35 years with a BMI of 21-30 kg/m². These participants will be randomly assigned to one of three groups:

1) Control group; “Self-guided behavior changes” (N=200)
2) Self-regulation with small behavior changes (N=200)
3) Self-regulation with large behavior changes (N=200)

Both self-regulation interventions will include an initial 4-month program and annual booster programs extending for up to three years. Participants will be enrolled over 2 years and will be followed from the time of randomization until the end of the grant, resulting in a planned 2-4 years of follow-up (mean of 3 years).

3.2 Specific Aims

The primary hypothesis of SNAP is that the magnitude of weight gain across an average planned follow-up of three years will differ among the three arms. Specific a priori hypotheses are that over an average of three years:

1. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus small behavior changes intervention compared to the control group.
2. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to the control group.
3. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to those assigned to the self-regulation plus small behavior changes intervention.

Secondary aims of SNAP are:

1. To compare the proportion of participants in the three groups (self-regulation plus small changes, self-regulation plus large changes, and control) who gain less than 1 pound over the planned follow-up of an average of three years;
2. To assess the mean differences in weight gain among intervention groups at 24 months post-randomization;
3. To compare the three groups on changes in behavior (e.g. diet, physical activity, abnormal eating behaviors, use of healthy and unhealthy weight control practices) and psychosocial measures (restraint, depression) over the average follow-up of three years;
4. To compare changes in cardiovascular disease risk factors (including blood pressure, lipids, insulin sensitivity, and waist circumference) across the three groups and examine the association of changes in cardiovascular disease risk factors with weight change and behavior changes;
5. To examine demographic and psychological variables that may moderate the effects of the interventions, including initial BMI, ethnicity, age, scores on the Eating Inventory, and treatment preference;
6. To examine potential mediators of the effect of the interventions, including changes in diet, physical activity, restraint, and change in self-regulatory behaviors; and
7. To compare the incidence rates of obesity (BMI > 30 kg/m²) and the proportions of participant who meet this criteria for obesity over time among the three groups.

We will also compare the intervention groups on measures of adherence to the self-regulation interventions, including attendance at meetings and submission of weight data and participants’ reports of their satisfaction with the interventions. DNA will be collected and stored for potential future use. The potential of developing a proposal to provide for extended post-trial follow-up will be assessed during the trial.
3.3 Sample Size Justification
SNAP is designed to provide ≥90% statistical power to detect average pairwise differences of 3.0 lbs between intervention arms; N=600 (N=200/arm) participants are projected to be sufficient for this goal. Group comparisons will be based on generalized linear models for longitudinal data. To estimate power, longitudinal weight change data (i.e. follow-up weight minus baseline weight in pounds) were simulated using covariances from Levine, et al,13 which yielded the following covariance matrix for weight changes at years 1, 2, and 3.

Table 3.3.1 Covariance matrix for changes in weight from baseline (lbs)

<table>
<thead>
<tr>
<th></th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>57.09</td>
<td>40.29</td>
<td>38.46</td>
</tr>
<tr>
<td>Year 2</td>
<td>40.29</td>
<td>124.99</td>
<td>78.23</td>
</tr>
<tr>
<td>Year 3</td>
<td>38.46</td>
<td>78.23</td>
<td>112.00</td>
</tr>
</tbody>
</table>

This covariance matrix was used to simulate (N=25,000) longitudinal data sequences (from a multivariate normal distribution, assuming these covariances hold for months 4, 12, and 24 and are constant for months 36 and 48. It was assumed that differences in weight changes among groups will be achieved by 4 months and maintained thereafter and contrasted this with models in which initial differences waned by an accruing 10% and 20% per follow-up visit. A loss to follow-up rate of 7.5% was applied at 4 months, an additional 7.5% at 12 months, and an additional 5%/yr thereafter.

Generalized linear models were fitted using maximum likelihood with unstructured covariance and tested whether the average weight loss over time varied among groups. Detectable mean differences in annual rates of weight gain between arms were projected, using a Bonferroni-adjustment (2-tailed significance level of 0.0167) to control for three pairwise comparisons. The accompanying table summarizes power projections for N=200/group for detecting a relative mean difference of 3.0 lbs at 4 months that is maintained or wanes over time. Also provided are power projections for relative intervention effects of 2.75 and 2.50 lbs.

Table 3.3.2 Projected Statistical Power for SNAP Trial

<table>
<thead>
<tr>
<th>Mean Treatment Effect at 4 Months</th>
<th>Statistical Power For Pairwise Comparisons: N=200/group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Constant 10% Waning 20% Waning</td>
</tr>
<tr>
<td>2.50 lbs</td>
<td>84% 79% 67%</td>
</tr>
<tr>
<td>2.75 lbs</td>
<td>91% 87% 83%</td>
</tr>
<tr>
<td>3.00 lbs</td>
<td>95% 93% 90%</td>
</tr>
</tbody>
</table>

How power is affected by different patterns of lost follow-up has also been explored: the above projections are reasonably robust across a range of assumptions.

SNAP will provide 90% power to detect a relative 28% reduction in the proportion of participants who gain weight over time. The statistical power afforded by N=200/group was projected by simulating strings of longitudinal data based on transition rates (to/fro weight gain) that were chosen to correspond to those reported by Levine, et al. A reasonable fit with a
Markov model was achieved in which the probability of weight gain during the first 4 months was 0.25 and, for each successive interval, the probability of transitioning to weight gain among those entering the interval without current weight gain was 0.40 and the probability of transitioning to no weight gain among those entering the interval with weight gain was 0.20. While this model may not have captured the full complexity of intra-individual patterns and correlation, it provided a good fit to the Levine data, particularly at Years 1 and 2. The model was extended through the four years of SNAP planned follow-up and generalized estimating equations (GEE) were used to project power. The intervention effect was defined as decreasing the probability of transitioning from no weight gain to weight gain by 28% and increasing the probability of transitioning from weight gain to no weight gain by 28%. From this N=200/group was projected to provide 94% power for each of the three (Bonferroni-adjusted) pairwise comparisons. A power of 72% is projected for the cross-sectional comparison of 36-month proportions.

4. STUDY POPULATION
SNAP targets the recruitment of 600 individuals who are aged 18–35 years and have a BMI of 21 – 30 kg/m². This age group was selected because young adults have the greatest risk of weight gain over time. The lower age cutoff of 18 years was selected since prior to this, many young adults are still living at home and thus are less responsible for food choices. Concerns about putative effects of the development of eating disorders are also greatest in younger students. The upper age cutoff of 35 years was selected because weight gain appears less common after this age.

The BMI range of 21 – 30 kg/m² was selected since weight gain prevention seems an appropriate message for these individuals. A BMI of 21 kg/m² was selected as the lower end of the eligibility criteria because individuals with a BMI of 21 kg/m² are able to lose 5-10 pounds and still remain within the normal weight range. (We will only recommend a 5 lb weight loss for individuals with a BMI of 21 to 24.9 kg/m² in the large changes condition, but have provided data in Appendix 1 showing that even if an individual with a BMI of 21 kg/m² loses 10 pounds, they will remain in the normal weight range). An upper cutoff of BMI=30 kg/m² was selected since individuals with BMI >30 kg/m² are considered obese, and weight loss (rather than weight gain prevention) is typically recommended for these individuals.14

SNAP has no restrictions with regard to gender, ethnicity, or race. It targets recruiting at least 25% men since both men and women are at risk of weight gain. It also targets recruiting at least 25% minorities, including African-Americans, Hispanic Americans, and American Indians since these groups are disproportionately affected by obesity and experience larger weight gains during young adulthood.3, 15

Exclusion criteria include:
1. Untreated hypertension, hyperlipidemia, or type 2 diabetes, unless permission is provided by their health care provider. We will advise individuals who have a fasting glucose >126 mg/dl, blood pressure levels >140/90 mmHg, pulse > 110 beats/min, triglycerides ≥ 500 mg/dl or LDL-C >160 mg/dl of these values and recommend that they contact their physician. Since weight control is an appropriate initial treatment for these medical issues, these individuals can participate in the trial if they receive permission from their
physician, and the physician indicates that he/she will be managing these risk factors. Participants who do not currently have a health care provider will be given a list of local providers.

2. Heart disease, heart problems, or participants who report being prescribed drugs for blood pressure or a major heart condition, unless permission is received from their primary care physician.

3. Type 1 diabetes or treatment of type 2 diabetes with insulin or oral medications that may cause hypoglycemia (e.g. sulphonylureas). These individuals will be excluded due to the concerns about hypoglycemia in a weight control program.

4. Health problems which may influence the ability to walk for physical activity (e.g. lower limb amputation) or other reasons why a person should not do physical activity, unless permission is provided from their health care provider.

5. Health problems that may be associated with unintentional weight change or affect the safety of a weight loss program, including report of a heart attack or stroke, chest pain during periods of activity or rest, loss of consciousness, active tuberculosis, HIV, chronic hepatitis B or C, inflammatory bowel disease requiring treatment within the past year, thyroid disease, renal disease, liver disease, hospitalization for asthma in the past year, or cancer within the past 5 years (except for non-melanoma skin cancers or early stage cervical cancer) or chronic use of steroid medication.

6. Report of a past diagnosis of or treatment for a DSM-IV-TR eating disorder (anorexia nervosa or bulimia nervosa) or meet criteria for anorexia or bulimia nervosa during screening for this trial

7. Report of a past diagnosis of or current symptoms of alcohol abuse or substance dependence

8. Currently pregnant, pregnant within the past 6 months, or planning to become pregnant within the next 6 months. These individuals may later be re-screened.

9. History of schizophrenia, manic depression, or bipolar disorder

10. Hospitalization for depression or other psychiatric disorder within the past 12 months

11. Having lost and maintained a weight loss of 10 pounds or more within the past 6 months or are currently participating in a weight loss program, trying to gain weight, using steroids for muscle mass or weight gain, taking weight loss medication, or have had surgery for weight loss

12. Participation in another weight loss or physical activity study that would interfere with this study

13. Another member of the household (or roommate) is a participant or staff member on this trial

14. Reason to suspect that the participant would not adhere to the study intervention or assessment schedule (i.e., can’t come to group on a regular basis; will be away for more than two weeks during initial intervention phase or planning to move from the area within next year)

15. Not able to speak and understand English

16. Residence or place of work further than 30 miles from the intervention site

17. Perceived inability to attend the intervention and assessment visits

18. No Internet access on a regular basis
Individuals who endorse on the Physical Activity Readiness Questionnaire (PAR-Q) either bone or joint problems, prescription medication usage, or other medical conditions that could limit exercise will be required to obtain written physician consent to participate.

5. RECRUITMENT and SCREENING
Participants will be recruited in cohorts of approximately 45 to 60 (15 to 20 randomized to each group) at the clinical sites. The general recruitment strategy for SNAP will be to use a multi-method strategy including advertisements in local media (television, newspapers, Internet, radio, etc.), direct mailings to young adults, and site-specific recruitment at locations where the target population likely live and work. These site-specific recruitment strategies include attending local meetings of young adult groups and making presentations or providing information to target specific worksites and universities in the metropolitan area of each study site. Where possible we will seek out opportunities to interact with local media about the general problem of weight gain in young adulthood and the long term, multi-center study that is available in the area to study the problem. We will conduct interviews and be available to local journalists to be interviewed for newspaper articles in various types of newspapers (student papers, local and regional papers etc.) or television programs.

In order to develop effective approaches for recruitment of both men and women for this trial, we have been conducting focus groups with young adults and asking specifically about recruitment messages and outlets. We will use this information to achieve our recruitment goals for men and women.

Both centers have prior experience recruiting minorities for weight loss studies. Investigators from the UNC have previously recruited successfully from several historically Black colleges in their area; investigators at the Miriam Hospital have recently conducted several weight loss programs for Latina women and developed excellent contacts within this community. For the most part, the types of strategies described above (television and direct mailings) have been found effective in recruiting minority participants. However, we will also consider advertisements in newspapers and on radio stations specifically focused on minority audiences, and recruitment efforts through local churches and community organizations.

Interested participants will be given basic information about the study by phone or via the study website and will complete an initial online screening form. Those who appear eligible will be further screened via phone interview and if eligible, invited to an orientation session during which the study will be reviewed in detail. The concept of random assignment will be described to the volunteers, as will the procedures for the assessment visits and the different treatment approaches given to each of the three arms of the study. Those who remain interested will be asked to review and sign the consent forms (see Appendix 2 for template of consent forms). Participants will then have their height and weight taken to check eligibility and will be scheduled for two screening visits. While specific measures are described for each screening visit, we recognize that the sequence of measures may be modified across visits to fit with participant’s schedules and development of the most effective procedural flow. We anticipate that at the first screening visit (conducted in the fasting state), the study staff will administer the Center for Epidemiologic Studies Depression (CES-D) Scale, blood pressures will be assessed and the phlebotomist will also take blood samples. Participants will be instructed in the
The goal will be to have participants record their activity for at least 8 hours per day on 4 of the 7 days (including 1 weekday and 1 weekend day). Participants will also be given information about how to complete self-report questionnaires about their medical history and health habits using an Internet based system. At Screening Visit 2, we will administer the Exercise Habits (Paffenbarger) Form and obtain baseline measures of height, weight, waist circumference, and body composition with the participant in a clinic gown. In addition, the questionnaires and SenseWear Pro arm-band data will be reviewed for completeness. The intervention and clinic staff will meet with the individual and complete a semi-structured interview in which the individual is asked to describe the purpose of the study and the various intervention groups to make certain that they understand the requirements of the trial. The interview will also include questions to assess the appropriateness of the individual for the trial and the timing of participation relative to other events in the individual’s life. Of greatest interest is making certain that the individual is willing to be randomized to any of the three groups in the trial. Each week, the study staff will meet and review the information about the potential participants. These procedures, including the completion of several days of monitoring activity, the interview, and the staff review of potential participants, have been very effective in selecting good study participants and reducing attrition from clinical trials. Those participants who seem appropriate for the trial will be called during the two weeks prior to randomization to ensure that they are still available and not pregnant and then will be randomly assigned to one of the three treatment groups.

6. RANDOMIZATION
A study website will be used for randomization, which will include an automatic check of the completeness and success of eligibility. Fall-back methods will also be in place, which allow for randomization via phone calls to the CoC if extended times without web service occur. The system prevents withdrawing participants after randomization has occurred and ensures concealment of the randomization scheme. To ensure blinding of the assessment staff to intervention assignment, randomization assignments will be obtained from the computerized data management system by staff who are not involved in height or weight assessments. In order for a participant to be randomized, he/she must have signed the informed consent, be in the eligible BMI and age categories, not report any of the health problems described above for ineligibility, have physician permission to join the study if deemed necessary based on health parameters (see eligibility), complete blood pressure and blood work for lipids, glucose, and insulin, successfully complete the behavioral interview, and report being available for the time/place that treatment is being conducted.

SNAP will adopt a simple, non-adaptive variable-block length randomization, which will ensure fairly equal allocations over time and make it difficult for staff to guess future assignments. Randomization will be stratified by clinical site to balance assignments on factors associated with each clinical site that are difficult to measure or quantify such as demography, geography, local health care personnel, local health care practices, clinical site personnel, and facilities. To ensure comparability of gender and ethnic representation across the three conditions, randomization will also be stratified by gender and ethnicity (Non-Hispanic white versus other race/ethnic groups). Extensive stratification is not recommended for a randomized controlled clinical trial of this size. Covariate adjustment can be used to address marked chance imbalances in measured pre-randomization characteristics.
7. RETENTION
Proactive efforts will be made to retain all participants for the entire study period including building strong rapport by sending participants birthday cards and periodic study newsletters. We will also obtain contact information (name, address, and phone number) of a family member or friend to assist in locating participants for follow-up assessments. These procedures have been used by investigators at both sites successfully with retention in recent clinical trials being 80-95% depending on point of follow-up and specific protocol.

A systematic protocol will be followed to minimize dropouts. Participants in the intervention will be called or sent an e-mail reminder before each session. If a participant has an unexcused absence, they will be contacted and helped to solve any barriers to attendance. The session materials will be e-mailed or sent to those who do not attend and make-up session will be offered. Top priority will be for assessment visits. The biggest source of dropouts in prior studies with this age group is pregnancy (15% of women in Health Hunters had a pregnancy; 11% of the women in POP). SNAP staff will stay in touch with women during pregnancy and allow them to return to the study at 6 months post-partum, we will continue to include their weight data in our analyses except during their actual pregnancy and the 6-months post-partum. However, individuals in their first trimester will be seen for assessment visits, but will not participate in the intervention because it may be contraindicated.

8. INTERVENTIONS
8.1 Control Condition (“Self-Guided behavior changes”)
The control/comparison condition (referred to as “Self-guided behavior changes”) will be used to determine the rate of weight gain over 3 years for individuals who are not given an active weight gain prevention intervention. The goal is to give participants in this condition minimal intervention (so as not to alter the natural history of weight gain) but to achieve maximal retention at the annual assessments. To accomplish this, a single face-to-face group educational session will be conducted soon after randomization and participants will be presented with basic education about weight gain in young adults, including information about the types of behavior changes associated with weight gain and the health consequences of weight gain. This session will educate the Control group about the importance of self-weighing as a preventive strategy and introduce them to both the small changes and large changes approaches, with the message that by providing them with information about both approaches we allow them to choose whichever approach they feel will work better for them. To help participants “self-guide” their own program of behavior change, they will be given the website for America on the Move and smallchanges.gov as a way to follow a “small changes” approach and several weight loss web links will be provided to illustrate a large changes approach. In addition, the Control group will have access to a study website where they can access quarterly newsletters covering weight gain prevention topics and providing healthy recipes and exercise strategies; however, although they are provided information and education, the control will not receive the assistance in implementing these approaches that is provided in the intervention groups.

8.2 Common Components of the Active Interventions
The two interventions tested in SNAP are comparable in the frequency of contact with the interventionist, the theoretical basis (i.e., self-regulation), the basic information provided about
healthy eating and physical activity, and the behavioral modification skills that participants are taught to help them make either small or big behavior changes.

8.2.1 Contact schedules
The initial intervention in both conditions consists of 8 weekly face-to-face group meetings and 2 monthly meetings (10 meetings over approximately 16 weeks), led by interventionists with backgrounds in nutrition, exercise physiology, or behavior modification and behavioral weight control experience.

Table 8.2.1.1 Intervention Contact Schedule

<table>
<thead>
<tr>
<th>Time Frame</th>
<th>Meetings</th>
<th>Reporting Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months 1-2</td>
<td>Weekly</td>
<td>None*</td>
</tr>
<tr>
<td>Months 3-4</td>
<td>Monthly</td>
<td>Weekly</td>
</tr>
<tr>
<td>Months 5-12</td>
<td>None</td>
<td>Monthly</td>
</tr>
<tr>
<td>Year 2</td>
<td>Annual 4 week refresher</td>
<td>Monthly</td>
</tr>
<tr>
<td>Year 3</td>
<td>Annual 4 week refresher</td>
<td>Monthly</td>
</tr>
</tbody>
</table>

*No reporting is needed since participants are weighed at weekly meetings

SNAP is conducting the intervention face-to-face because in prior studies, lower intensity approaches (e.g., newsletters; correspondence programs) have not been effective in preventing weight gain in young adults. The only programs that have met with any success have been more intensive and involved face-to-face contact. Likewise face-to-face was more effective than Internet in preventing weight regain. SNAP will use a moderate intensity program with weekly meetings for the first 2 months and monthly for the second 2 months. Groups will be conducted in a closed format with approximately 20 members (i.e., the 20 participants will start and end these 10 meetings together). In subsequent years (ranging from 2-4 additional years due to the planned staggered enrollment), participants will be offered an annual 4-week refresher program. Participants will not need to stay with their original cohort for these refresher courses. Several sessions will be offered on different days and times, and participants will be able to choose the one that is most convenient for them. This concept of using open format refresher courses/campaigns was used successfully in the Diabetes Prevention Program and is being used currently in Look AHEAD. The proposed intervention schedule was selected with awareness of the busy lives of young adults and as appropriate for future implementation in real-world settings, such as YMCAs, employee health programs, or health clubs. In addition, make-up sessions will be offered (and attendance at these documented) and all materials will be available on the study website to help those who are unable to attend a specific session of the program.

To maintain contact with participants between meetings and to increase accountability, SNAP will supplement face-to-face meetings with use of a web-based system that participants will use to report their weight and behaviors.

8.2.2 Intervention delivery
The goal of both interventions is to prevent weight gain through the self-regulation of eating and exercise behaviors, a model that was used successfully in STOP Regain. All of the basic
elements are used again in this weight gain prevention program. Participants will be given scales for use at home and will be taught: a) to weigh themselves daily; b) to detect small changes in weight as soon as they occur; c) to implement problem solving strategies to deal with these changes; d) to evaluate the success of these strategies; and e) to provide self-reinforcement for successful weight maintenance or to make changes in their behavior if gains occur.

To help participants detect small changes in their weight and to guide appropriate actions, they will be taught to use a red, yellow, and green weight monitoring system. Participants will use a web-based system to report their weight on the contact schedule outlined above; based on their reported weight, they will receive feedback as to their color zone for the week (see color zone descriptions below) and will be instructed to practice either reinforcing themselves or taking the corrective appropriate action. The color zones for both interventions will be identical.

**The “green zone” (Go!):** at or below their weight at the end of the initial intervention. Participants whose weight is in the green zone will be encouraged to reinforce themselves for their success. To teach such reinforcement, the study will initially provide small token reinforcement for participants in the green zone on a preset intermittent schedule, the equivalent of once per month (e.g. green tea, green dollar bill, green Frisbee). These token reinforcers were very well received in Stop Regain and our pilot for this trial.

**The yellow”(Caution!) zone:** weight is above the participant’s weight at the end of the program but below their starting weight. Participants who are in the yellow zone will be warned that their weight is creeping up, with increasing intensity of the warning as they come closer to the red zone. They will be taught to return to self-monitoring of diet and activity, to identify behavior changes that may be causing the weight gain, and to use problem solving strategies to reverse these changes. Thus, behavior changes are recommended in response to any weight regain, with more urgent recommendations if weight approaches the red zone.

**The “red” (Stop!) zone:** any weight above the participants’ starting weight. If participants enter the red zone, more substantial changes in behavior will be prescribed (this action plan differs by treatment condition – described below). In addition, participants in the red zone at the end of the month will be asked if they would like additional help from a counselor either via phone, e-mail, or in person. Up to two individual sessions will be made available to participants during any month that they are in the red zone.

A structured protocol will be used for these individual Red counseling sessions and all contacts will be documented in the study data system. The sessions will be conducted by a nutritionist or individual experienced in behavioral weight control; the participants will speak with the same interventionist whenever possible to provide continuity of care. The contact will last about 20 minutes and have two parts—an introductory/motivational portion and a goal setting portion. The introductory portion will be based on motivational interviewing and will be similar for participants in the large and small change groups; the participant will be encouraged to reflect on their reasons for joining the study and their initial desire to prevent weight gain. Discrepancies between these initial goals and their current behavior will be discussed. The second part of the call will clearly differ by treatment group. The participant will be encouraged to consider ways in which they could stop their weight gain – using the type of techniques they have previously been taught (i.e. small or large changes, see below). For example in the Large Changes group,
the participants will be encouraged to consider strategies such as returning to self-monitoring or to a calorie-controlled diet or rejoining a gym; in contrast, the Small Changes group would be encouraged to resume wearing their pedometer and to think about making an additional small change in their diet. At the end of the contact, the interventionist will complete a report indicating the types of contact (phone; e-mail; in-person), the issues discussed and the participant’s plan. This contact form will be useful in guiding subsequent contacts (to inquire about progress toward goals set on the last call), but also will provide important process data for the trial.

8.2.3 Modifying eating behaviors
Both intervention groups will be taught about energy balance and how body weight relates to energy intake and expenditure. They will also learn about appropriate portion sizes and the calories in protein, fat, and carbohydrates, and will be taught basic nutrition skills such as label reading. Participants in both groups will be encouraged to consume a heart healthy diet, with a low intake of saturated fat and trans-fats and high intake of fruits, vegetables and whole grains. Prior studies have shown that weight gain in young adults is associated with increased caloric intake and percent fat; changes in dietary pattern toward a more “prudent” dietary pattern and away from a Western pattern have also been associated with lower weight gains and thus will be encouraged in the program.

Specific attention will be devoted to those aspects of eating behavior that have been related to weight gain in young adults, particularly fast food consumption, alcohol consumption, and sweetened beverages.

8.2.4 Modifying physical activity
Both interventions will also emphasize the importance of increasing physical activity and decreasing sedentary behaviors as a means of preventing weight gain. General information about the calories burned in different types of activity will be presented to both intervention groups and the importance of both programmed and lifestyle physical activity will be stressed. The program will strongly emphasize physical activity since young adults are at risk for decreasing their physical activity and changes in physical activity level and physical fitness have consistently been associated with both weight gain over time and with weight regain after initial weight loss. The interventions will also seek to decrease time spent in sedentary activity since again, this has been related to weight change in young adults.

8.2.5 Behavior modification skills
In addition to education about healthy eating and physical activity, participants in both groups will receive instruction in core cognitive and behavioral skills such as self-monitoring, stimulus control, problem solving, social support and assertiveness training, goal setting, and cognitive restructuring to help them implement their small or large behavior changes.

8.3 Differences Between the Two Active Interventions.
The differences in the two active interventions are summarized in Table 8.3 and described in detail below.
Table 8.3.1: Treatment Components that Differ between the Two Intervention Groups

<table>
<thead>
<tr>
<th>Key Intervention Concepts</th>
<th>Small Changes</th>
<th>Large Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary changes recommended for maintaining weight (green zone)</td>
<td>Instructed to make one small change in diet every day</td>
<td>Start with 1200-1800 kcal/day diet to create weight loss buffer in first 8 weeks. After buffer created, gradually increase caloric intake until maintaining weight loss, but continue to consume low calorie, low fat healthy diet</td>
</tr>
<tr>
<td>Physical activity changes recommended for maintaining weight (green zone)</td>
<td>Given pedometers and instructed to increase steps by 2000 steps per day over baseline levels and maintain this level</td>
<td>Instructed to exercise for 250 min/week (50 min/day on 5 days/week) throughout the entire program.</td>
</tr>
<tr>
<td>Self-monitoring of behavior changes</td>
<td>During initial 12 weeks and for refresher courses, record number of steps per day and check off whether or not a small change in diet was made every day. Self-monitor weight daily throughout the entire program.</td>
<td>Self-monitor food intake (calories and fat grams) for first 12 weeks of the program, throughout the refresher course, and if they experience weight regain. Self-monitor weight daily throughout the entire program.</td>
</tr>
<tr>
<td>What to do if regain 1 pound or more above the weight they achieve at the end of initial 8 week program, but remain below baseline (yellow zone)</td>
<td>Taught to resume self-monitoring of steps and small changes to diet. Use problem-solving skills, with an emphasis on changing surrounding environment to support small changes.</td>
<td>Taught to resume self-monitoring of food intake for several days to help identify problem areas and get back on track. Use problem-solving skills, with an emphasis on changing surrounding environment to support big changes.</td>
</tr>
<tr>
<td>What to do if exceed baseline or starting (red zone)</td>
<td>Instructed to implement additional small change(s) in both eating and exercise (e.g. make at least 2 small changes in intake each day and increase steps by 3000 over baseline level). Given toolbox containing suggestions for different types of small changes that can be made in diet and physical activity. Continue to make additional small changes until weight is back to the green zone.</td>
<td>Instructed to reinitiate big changes – return to 1200-1800 kcal/day diet, continue 250 min/week of activity, and self-monitor intake and activity until they are back in the green zone. Given toolbox containing extra self-monitoring diaries, meal plans, meal replacements to help create weight loss buffer.</td>
</tr>
</tbody>
</table>

8.3.1 Self-regulation plus small behavior changes

The Self-Regulation Plus Small Behavior Changes Intervention will focus on making small changes in diet and physical activity on a daily basis to prevent weight gain (see Appendix 3 for sample sessions). Participants will be taught that by making one small change in how much they eat or what they eat and increasing their physical activity by 2000 steps per day, they can prevent weight gain and perhaps even lose some weight. The initial program will help participants identify and practice these small changes which they will continue to implement on a consistent, permanent basis to prevent weight gain.

Diet: The dietary approach used in this group is to identify small changes in what and how much participants eat each day. Although these changes are described as being approximately 100 calories, it is recognized that the calorie value of each specific dietary change will vary;
rather, the general concept is that these are small, manageable changes that will produce small reductions in overall intake and can easily be made on a daily basis and maintained over time. Participants will be first introduced to the strategy of reducing the amount (portion size) of foods consumed. Specific strategies (many from America on the Move) will be suggested, including for example, leaving 3 – 4 bites of food on their plate, using only 1 slice of bread for an “open-faced sandwich.” Participants will be given a list of these strategies and asked to try one strategy each day. In subsequent weeks, participants will be introduced to small changes they can make to modify the types of food they eat; small changes when eating out and small changes in liquid calories, two areas that are particularly challenging for young adults, will also be presented. For each type of diet change, the group will brainstorm possible small changes that could be made and a list of suggestions will be provided to participants.

**Exercise:** At the start of the program, participants will be given a pedometer and asked to record their current or baseline number of steps. They will then be given the goal of increasing their daily steps by 2000 steps per day over this baseline level. The group will brainstorm ways to increase daily steps and participants will be given a handout reviewing such strategies (many of these suggestions come from America on the Move). Participants will be instructed to select a small change they can make each day in order to increase their overall steps by 2000. At the subsequent meeting, their success at implementing this behavior change strategy will be discussed. If the participant selects a strategy that does not increase activity by 2000 steps, an additional small change will be suggested. Lifestyle changes (walking the dog; mowing the lawn) will be stressed as one way to increase exercise by 2000 steps, but the approach of adding additional minutes to structured exercise (bike riding for 10 minutes more) will be discussed at subsequent meetings.

**Self-monitoring:** Participants will be given a monthly chart to use to record their daily weight and the number of steps they take each day. In addition, they will check a box to indicate whether they made a small change in their diet during that day. The Small Changes group will complete this record of weight, steps, and whether a change in diet was made every day throughout the first 12 weeks of the program and the refresher course. These participants will be instructed to record their weight daily throughout the entire trial. If they enter the “yellow” zone, they will resume monitoring of small changes in diet and pedometer steps.

**Maintenance:** During the initial program, participants will try a variety of ways to decrease calorie intake and increase exercise. Subsequently they will be instructed to select from these strategies each day and continue to make one change in diet each day and one or more changes in activity to increase steps by 2000. If these participants experience weight gains at any time over the three years (i.e. enter the yellow zone), they will be taught to immediately return to self-monitoring of diet and exercise using their pedometer and the monthly chart to confirm that they are still making small changes in diet and achieving their step goal. They will be taught to problem solve about the causes of the weight gain. If these actions are not sufficient and weight regain continues or they enter the red zone, they will be taught to add an additional small change in both diet and activity. By making several small changes, these participants will be gradually altering their energy balance (two small activity and two small diet changes equals approximately a 400 calorie deficit which should produce almost a 1 pound/week weight loss). In addition, during the initial intervention, they will create a “toolbox” that they will be able to
use if they experience weight gain. Finally, when in the red zone, participants will be encouraged to contact the program staff for additional counseling and guidance.

**Refresher courses:** At each annual refresher course, members of this group will be asked to again monitor their steps and check off whether they are making a small change in diet each day. As described above, participants who have experienced weight gains will be encouraged to increase to two small changes in eating each day and to a step level of 3000 steps over baseline. In addition, the refresher program will include a physical activity or a nutrition activity that will be fun for participants and help motivate attendance and weight control.

**8.3.2 Self-regulation plus large behavior changes group**

The focus of this intervention group will be on periodically making large changes in diet and physical activity, with the goal of losing 5-10 pounds to buffer against the weight gain that often occurs during young adulthood. Recognizing that it is challenging for young adults to pay close attention to diet and exercise at all times, this group will be encouraged to spend a few weeks each year really focusing on diet and exercise to produce a 5-10 pound weight loss, and then throughout the rest of the year, focus on weighing themselves regularly and maintaining healthy eating habits and high physical activity levels to prevent weight regain.

**Diet:** Individuals with a BMI of 21-24.9 kg/m² will be encouraged to lose 5 pounds; those with a BMI of 25-30 kg/m² will be encouraged to lose 10 pounds. To produce these weight losses, participants in the Large Changes group will be instructed to consume either 1200-1500 or 1500-1800 calories per day, with <30% of calories from fat. The specific calorie range will be individualized for participants based on their weight and the amount of physical activity they report during baseline assessments. To stay within their recommended calorie range, participants will be taught about calorie balance and about the calorie content of different types of foods. They will be given specific meal plans modeling a low calorie low fat eating plan that they can use since this type of structure has been shown to improve weight loss. They will continue to follow the 1200-1500 or 1500-1800 calorie diet until they achieve the 5-10 pound weight loss goal, which we expect will occur for many by the end of the initial 8 week program; after reaching their weight loss goal, their calories will be gradually increased to maintain this reduced weight level and a healthy, low calorie, low fat regimen will be encouraged. The period between weeks 8 and 16 will provide an opportunity for these participants to determine the calorie level they need in order to maintain the 5 to 10 pound weight loss.

**Exercise:** The Large Changes group will be instructed to gradually increase their minutes of physical activity until achieving 250 minutes per week (5 days/week with 50 minutes per day) using activities similar in intensity to brisk walking. Since this high level of physical activity has been shown to be important for weight loss maintenance, participants in the Large Changes group will be taught to maintain this high level of activity over all subsequent years of the program.

**Self-monitoring:** During the first 12 weeks (and during each refresher course), the Large Changes group will record their weight and the specific foods they eat each day, including portion sizes, and the number of calories and fat grams in those foods and their minutes of physical activity. They will continue to record their weight throughout the trial.
Maintenance: After completing the initial program, the primary emphasis will be on monitoring weight on a daily basis and using the weight data to determine if and when behavior changes are needed. Individuals who start to regain weight after the initial program, but do not exceed their baseline weight (i.e. in the “yellow” zone) will be instructed to return to self-monitoring their diet and exercise and to problem solve and to identify behavior changes that may be related to their weight gain. It is anticipated that there will be variability in the weight losses achieved by participants in the Large Changes group during the initial phase of the program, and thus differences in the amount of weight the person can regain before approaching their baseline weight. Thus, persons who lose more weight initially will have created a wider “yellow” or caution zone (i.e., a wider “buffer”) for themselves. If these participants continue to regain within the yellow zone, and begin to approach the red zone, they will receive more urgent messages to take steps to get back on track. If these participants enter the red zone, they will be taught to return to the reduced calorie intake goal of 1200 – 1500 or 1500 – 1800 calories per day. They will be encouraged to use the structured meal plans and meal replacement products to achieve these goals. In addition, they will make certain that they are reaching the 250 minute activity goal, and if needed, increase above this level. If these participants enter the red zone, they will be encouraged to contact the program staff for counseling session.

Refresher Courses: The refresher courses will be 4 weeks in a row and will be used to help participants return to their 5-10 pound below baseline level. Again, a calorie and physical activity prescriptions and daily self-monitoring will be important aspects of the program. Individuals who have maintained their initial weight loss will be allowed to lose more weight if they wish, provided that they do not reduce below a BMI of 18.5 kg/m² (the lower end of the normal BMI range). The refresher classes offered to this group will include cooking demonstrations and fitness activities to provide educational and interactive ways to encourage maintenance of the 5-10 pound weight gain buffer.

9. DATA COLLECTION
9.1 Assessments
All assessments will be completed by staff members who are blinded to the participants’ intervention assignment and have been certified by the Coordinating Center in the appropriate conduct of the measures. Participants will be provided a $50 honorarium for attending each assessment session. Table 9.1 shows the schedule of assessments for SNAP.
<table>
<thead>
<tr>
<th>Measure</th>
<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Anthropomorphic</strong></td>
<td></td>
</tr>
<tr>
<td>Weight (primary outcome)</td>
<td>X</td>
</tr>
<tr>
<td>Height</td>
<td>X</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>X</td>
</tr>
<tr>
<td>Body composition with impedance</td>
<td>X</td>
</tr>
<tr>
<td>Body composition with BodPod (UNC only)</td>
<td>X</td>
</tr>
<tr>
<td><strong>Behavioral and cognitive</strong></td>
<td></td>
</tr>
<tr>
<td>Diet (Food Frequency Questionnaire)</td>
<td>X</td>
</tr>
<tr>
<td>Specific questions about diet</td>
<td>X</td>
</tr>
<tr>
<td>Physical activity: Paffenbarger</td>
<td>X</td>
</tr>
<tr>
<td>Sedentary Activity</td>
<td>X</td>
</tr>
<tr>
<td>Objective (arm bands)</td>
<td>X</td>
</tr>
<tr>
<td>Weight history</td>
<td>X</td>
</tr>
<tr>
<td>Weight management strategies</td>
<td>X</td>
</tr>
<tr>
<td>Self-weighing</td>
<td>X</td>
</tr>
<tr>
<td>Eating disorders assessment</td>
<td>X</td>
</tr>
<tr>
<td>Eating Inventory</td>
<td>X</td>
</tr>
<tr>
<td>Autonomous motivation</td>
<td>X</td>
</tr>
<tr>
<td>Smoking, alcohol use</td>
<td>X</td>
</tr>
<tr>
<td>Sleep Habits</td>
<td>X</td>
</tr>
<tr>
<td>Neighborhood, environment</td>
<td>X</td>
</tr>
<tr>
<td><strong>Medical</strong></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
</tr>
<tr>
<td>Fasting lipids, glucose, insulin</td>
<td>X</td>
</tr>
<tr>
<td>Medication use</td>
<td>X</td>
</tr>
<tr>
<td>Medical events</td>
<td>X</td>
</tr>
<tr>
<td>DNA, serum, plasma</td>
<td>X</td>
</tr>
<tr>
<td><strong>Psychological assessments</strong></td>
<td></td>
</tr>
<tr>
<td>Depression (CES-D)</td>
<td>X</td>
</tr>
<tr>
<td>Life events</td>
<td>X</td>
</tr>
<tr>
<td>Perceived stress</td>
<td>X</td>
</tr>
<tr>
<td>Quality of life</td>
<td>X</td>
</tr>
<tr>
<td><strong>Other questionnaires</strong></td>
<td></td>
</tr>
<tr>
<td>Demographic data</td>
<td>X</td>
</tr>
<tr>
<td>Contact Information</td>
<td>X</td>
</tr>
<tr>
<td>Weight status of friends and family</td>
<td>X</td>
</tr>
<tr>
<td>Treatment preference, satisfaction and post-treatment feedback</td>
<td>X</td>
</tr>
<tr>
<td><strong>Adherence (Intervention groups only)</strong></td>
<td></td>
</tr>
<tr>
<td>Attendance at adherence sessions</td>
<td>Throughout</td>
</tr>
<tr>
<td>Weekly submission of weight data</td>
<td>Throughout</td>
</tr>
</tbody>
</table>
9.1.2 Anthropometric measures

- **Weight** will be measured in light clothing or a hospital gown, without shoes, on calibrated scales at each assessment visit. Two measures will be completed and the average of the two will be used. If the difference between the two measures exceeds 0.2 kg, a third measure will be taken.

- **Height** will be determined at each assessment visit using a wall mounted stadiometer. Two measures of height will be taken and the average of the two will be used. If the two measures are not within 0.5 cm, a third measurement will be taken. We will repeat the measurement of height at each assessment visit because growth may still be occurring in these young adults. The weight and height measures will be used to calculate Body Mass Index (weight in kilograms divided by height in meters squared).

- **Waist circumference** will be measured using a Gulik tape measure and following a standardized protocol. Two measures of waist circumference will be taken; if the difference exceeds 1.0 cm, a third measure will be taken.

- **Body composition.** Both sites will complete measures of body composition with the RJL Systems Quantum II impedance machine. In addition, participants at UNC will also have body composition assessed with the BodPod. Participants will be asked to fast for 4 hours, refrain from alcohol for at least 12 hours, and to refrain from strenuous exercise or sauna for 8 hours prior to these measures.

9.1.3 Behavioral and cognitive measures

**Diet.** Dietary intake will be assessed at baseline, month 4 and month 24 with the Block Food Frequency Questionnaire (FFQ), a semi-quantitative food frequency questionnaire that has been used in a number of weight loss intervention trials including Look AHEAD, DPP, and PRIDE. For each food item on the Food Frequency, participants report the frequency of consumption and the portion sizes consumed over the past month. The FFQ assesses the consumption of low fat versions of 10 foods, including meats, cheeses, yogurts, and cookies/cakes and has been modified to include liquid meal replacement products and ethnic food choices. An important reason for selecting this approach to dietary assessment is that the participants can complete the FFQ on-line at their own convenience.

Data from the FFQ will be supplemented with several diet and eating behavior questions that can be asked at each assessment visit. These will include items related to frequency of meals at fast food restaurants, frequency of meals at other types of restaurants, and consumption of sweetened beverages.

**Physical Activity.** The Paffenbarger Activity Questionnaire (PAQ) will be administered as a measure of physical activity at each assessment visit. The PAQ has been used to assess leisure time activity in many weight loss trials and can be scored to provide an estimate of calories expended per week in overall leisure time activity and in activities of light (5 kcal/min), medium (7.5 kcal/min), and high (10 kcal/min) intensity. Changes in exercise on the PAQ have been shown to be predictive of weight change in overweight and obese individuals.

Given the increasing recognition of the importance of sedentary activity, independent of physical activity, we will assess sedentary activity at each assessment visit using a self-report
questionnaire, which asks respondents to indicate the number of hours they spend on a typical weekday and a typical weekend day doing a variety of sedentary activities.

We will also include an objective assessment of physical activity at baseline, month 4, month 12, and month 24 in order to confirm the self-report data and to determine whether participants in the small and large changes conditions have different patterns of activity that reflect the different exercise recommendations given to the two groups (e.g. longer bouts of activity in the large changes condition). We will use the SenseWear Pro Armbands (Body Media, Pittsburgh PA) in this trial. The Sense-Wear Pro Armband is a newly developed commercially available device to assess energy expenditure. The device, worn on the upper arm, uses data from a variety of parameters, including heat flux, accelerometer, galvanic skin response, skin temperature, near-body temperature, and demographic characteristics to estimate energy expenditure using proprietary equations developed by the manufacturer. The novel technology of a heat flux sensor appears to make it more accurate than prior technology in assessing expenditure. Investigators at both sites have utilized these instruments in prior studies and thus are familiar with the technology.36 Participants will be instructed to wear the device during all waking hours (except swimming and showering) for a full week; monitoring for at least 8 hours per day for at least 4 days in the week (including at least one weekday and one weekend day) will be considered adequate for analysis. Weight History. Participants will complete a questionnaire reporting their weight history, including information about why they joined the program, highest and lowest weight, and weight at key age intervals.

Weight Management Strategies. We will assess both healthy (e.g. record what you eat daily, cut out between meal snacking) and unhealthy (e.g. take diet pills, fasting) weight control practices using questions compiled from Pound of Prevention,21 NHANES and the Weight Loss Maintenance trial. Participants will be asked to indicate whether or not they used they have used each strategies within the past 4 months, and if so, to indicate how frequently they used the strategy. Participants will also indicate whether they have participated in any other commercial weight loss programs including commercial and Internet programs and/or followed any other weight loss diets (e.g. Atkins).

Frequent self-weighing is the pivotal component of self-regulation. To assess this, participants will be asked to indicate how frequently they have weighed themselves, ranging from several times a day, daily, a few times a week, weekly, once a month, or less than once a month to never. Participants will also be asked to indicate the extent to which they found weighing themselves to be frustrating or motivating and how they reacted if they observed weight gains.

Eating Disorders Assessment (EDA). Participants will complete a questionnaire used in Look AHEAD that assesses the frequency of binge eating episodes accompanied by loss of control, and the frequency of compensatory behaviors including vomiting, diuretics, and fasting. These data will be used to identify any individuals who meet criteria for bulimia nervosa during the trial.

Eating Inventory. The Eating Inventory (TFEQ)37 is a 51-item self-report instrument with three factors, assessing dietary restraint, disinhibition and hunger. The Restraint factor (range 0-21) assesses the degree of conscious control one is exerting over eating behaviors. This factor has been related to successful weight loss and maintenance.38 The Disinhibition factor (range 0-16)
measures susceptibility to loss of control over eating; this factor has been shown to correlate positively with frequency and severity of binge eating. Scores on the hunger factor range from 0-14; different diet prescriptions within weight loss interventions have been shown to influence scores on the hunger factor.

**Autonomous Motivation.** Autonomous motivation for preventing weight gain will be measured with the Treatment Self Regulation Questionnaire. Half of the items reflect autonomous motivation (e.g., “Because I feel that I want to take responsibility for my own health”) and half reflect controlled motivation (e.g., “Because I would feel guilty or ashamed of myself if I did not try to control my weight”). Participants will rate each item using a 7-point Likert scale ranging from 1 “not at all true” to 7 “very true.” We have recently reported that increases in autonomous motivation were associated with better weight loss. The Small Changes intervention, by focusing on self-selected changes in diet and exercise, may foster autonomous motivation for behavior change, which may in turn be associated with better weight maintenance.

**Smoking and Alcohol.** Questionnaires will be administered at baseline and at each assessment to assess smoking and alcohol behaviors and any changes that occur over time.

**Sleep Habits.** A questionnaire will be administered at each assessment that asks about duration of sleep and problems encountered during sleep (e.g. snoring).

**Neighborhood, environment.** A questionnaire will be administered at each assessment that asks about the neighborhood and environment and the facilities that are available.

### 9.1.4 Clinical measures

**Blood pressure** will be assessed with a Dinamap Monitor Pro 100. Cuff size will be determined by arm circumference. Three readings will be taken, with a 30-second wait between.

**Fasting blood samples** will be taken for analysis of lipids (total cholesterol, HDL-C, LDL-C and triglycerides) and glucose and insulin levels at baseline and month 24. In addition, we will store baseline and 24 month samples of serum and plasma for later analysis for additional phenotypic markers of cardiovascular disease risk, such as inflammatory markers. These measures are collected to examine changes in specific risk factors and in the metabolic syndrome.

**Medication Use.** At baseline and each assessment, participants will be asked to report all prescription and non-prescription medications.

**Medical events** and symptoms will be collected at each assessment visit after baseline, using a standard form that is administered by study staff. Any positive responses will be reviewed by appropriate study personnel to determine if an SAE form is required.

**DNA** will be collected at baseline or month 24 to enable future studies to capitalize on a well-characterized group of young adults enrolled in a randomized, controlled trial that will allow testing of interactions between treatment group and genetic variations. By banking the DNA, SNAP will have the maximum flexibility to select a genetic study design and potential candidate genes that reflect the state of the art as the trial is completed.
9.1.5 Psychological assessments

**Depression.** The Center for Epidemiologic Studies Depression Scale (CES-D)\(^{35}\) is a self-report depression scale designed to measure depression symptoms in the general population. The self-test measure includes 20 items that relate to feelings and behaviors during the past week. The CES-D will be administered at baseline and each assessment visit to determine whether the interventions are associated with improvements or worsening in mood relative to the control.

**Life Events.** The life events questionnaire from the CARDIA study lists 67 events and participants are asked to indicate whether or not that event has occurred in the past year. We have chosen to use the CARDIA life events questionnaire in preference to other similar questionnaires (e.g. Holmes and Rahe)\(^{46}\) because it was developed specifically for young adults and reflects the type of life events that occur most commonly in this age group.

**Perceived Stress.** The Cohen Perceived Stress Scale\(^{47}\) is a 4-item self-report instrument that captures the participant’s perception of stress in their lives over the past month. The Perceived Stress Scale poses general questions about current stress levels. All items begin with the phrase: In the past month, how often have you felt…? This instrument has been used in many studies and has excellent reliability and validity.\(^{47,48}\)

**Quality of Life.** All participants will complete the CDC Health-Related Quality of Life measure (commonly referred to as “Healthy Days Measures”) at each assessment. This 4 item questionnaire has been utilized in the BRFSS and NHANES and has been shown to have appropriate reliability, validity, and responsiveness to change.

9.1.6 Supporting measures

**Basic demographic information** will be collected, including age, race/ethnicity, occupation; education and prior experience in weight loss programs.

Connection information will be collected at baseline and each assessment visit in order to assist clinic staff with retention.

**Weight Status of Friends and Family.** Based on the increasing recognition of the importance of social networks, we will ask participants to indicate the weight status of their friends and family members. This information will be collected at each assessment visit to determine if changes in weight in the participant are related to the weight status of others in their social network.

**Treatment Preference and Satisfaction.** Prior to randomization, each participants’ preference for and perception of each of the three arms of the trial will be recorded to determine whether initial preference for small or large changes group relates to outcome in participants assigned to their preferred or non-preferred alternative. Participants will also complete a post-treatment process evaluation including describing the perception of the program. This information will provide a more complete picture of how SNAP interventions are perceived and experienced by young adults and may provide valuable information about how to modify the programs for future use in this population.
9.1.7 Measures of adherence
Data will be collected on the number of intervention visits attended in the two active intervention
groups. Attendance at treatment sessions is anticipated to decline over time, but in keeping with
prior studies in the weight control literature, those who attend more sessions are expected to
have better weight loss outcomes. Data will also be collected on any individual make-up
sessions attended and individual “red-zone” counseling sessions.

Participants in the intervention groups will be instructed to report their weight weekly via the
study website. These data will be tabulated to derive a measure of percent of weeks in which
weight was reported. In STOP Regain, attendance and weight reporting were significantly
correlated with each other, and weight reporting was associated with successful maintenance of
weight loss.9

9.1.8 Measures of intervention fidelity
To ensure that the interventions delivered to the Small Changes and Large Changes groups
remain distinct from each other and appropriately reflect the intervention protocol, all
intervention sessions will be audiotaped. A random 20% of these sessions will be selected for
review by an interventionist or investigator who is not involved in this specific wave and is
masked as to which group is being conducted. The reviewer will listen to the session tape and
complete a written form indicating whether it was a small or large change intervention session
and indicate the basic message provided to participants about the diet, physical activity, and the
weight change goal of the intervention.

10. DATA MANAGEMENT and QUALITY CONTROL
10.1 Data Management
The SNAP web-based data entry system allows for direct data entry by participants and entry by
staff from data collected on paper forms. Data entered into the system are immediately available
for review and reporting. Participants will have the option to enter select forms directly into the
website prior to their clinic visit.

10.2 Monitoring Data Quality
Online reports will be used to provide up-to-the-minute access to data. Regular reports will also
be sent to the Steering Committee, and a subset of these will be continually updated on the study
website. These will allow the study to verify completeness, timeliness, reliability, and accuracy
of collection and coding of its data. The quality reports include comprehensive data on all
quality control activities, including protocol adherence and violation, training, retraining and
certification, site visit reporting, and data from monitoring the distribution of individual values
and of mean or median values by Clinical Site. Included will be comparisons of measures of
distribution of values over time and between Clinical Sites. The Coordinating Center will
develop and maintain standards to identify outlying values, and initiate and coordinate separate
review of these observations for accuracy.

10.3 Website and Security
The SNAP website is the foundation of its coordination, communication, management, data
entry and transmission, quality control, and distribution of information. It is a web-based
application comprised of a Microsoft-based web server which runs Adobe’s ColdFusion
application server for integration of the database information with the web site. All data reside in a Microsoft SQL Server database server managed by Public Health Sciences. The database is restricted so that only the database administrators and designated project representatives are able to access the information. The web application itself requires a correct username and password for login and implements role-based security to prevent unauthorized access to or manipulation of confidential information. The system allows authorized individuals to access participant information for the purpose of completing the project requirements. Audit logs are maintained which identify the activity of each user at all times while logged into the system and will capture and store each version of every record that is saved on the system. Users who access the system, once authenticated, establish a secure SSL encrypted session and all transmissions will then be encrypted until they logout or close the browser. Any transfer of data outside the Coordinating Center is done securely. Secure internet transfers (secure FTP or encrypted webpage downloads) within the study will contain only the necessary identifying data.

Both the database and application are backed up nightly onto dedicated backup storage with periodic backups stored offsite in Information Services long term backup vault.

10.4 Quality Control
Quality assurance and quality control are shared responsibilities among the SNAP team of investigators. The validity and eventual acceptability of study results depend in part on maintaining data integrity, documenting dropouts, monitoring and assessing protocol adherence, and unbiased measurements. The quality control program includes reviews of questionnaires, and duplicate measurements for instrument based work (e.g., anthropometry, blood pressure). The goal of all quality control work is to maintain a high degree of data quality throughout the course of the study and to document study quality for publications.

Of the many possible sources of heterogeneity between Clinical Sites, one of the largest and most controllable is uniformity in the application of the protocol. Central training, staff certification and site visits will be used to enhance standardization across the Clinical Sites.

A detailed and complete Manual of Operations is necessary for a successful study. The Manual of Operations serves as the study-wide procedural handbook and contains detailed information describing every aspect of the study including thorough descriptions of procedures for recruitment, clinical and lab measurements, data collection and handling, monitoring and follow-up.

The web-based system will be used to generate and resolve data queries. It provides an immediate correction to the database, creates a reliable audit trail, and minimizes duplicate requests for data cleaning to the clinics. Clinical Sites will receive regular reports on missing and incomplete forms and results of quality assurance checks.

Secure web-based file uploads that include basic data checks are used for quality assurance for Central Laboratory, Food Frequency, Bod Pod, Intervention and Accelerometry data. Further checking occurs when uploaded files are converted into SQL databases. The Coordinating Center will maintain logs of data received from all sources, and pursue missing data and correctable errors.
Standardized procedures for measuring cardiovascular disease risk factors are an important part of the quality process. The Study Group and Central Laboratory will define local blood collection and processing requirements, and develop training and certification procedures for Clinical Site staff.

11. PARTICIPANT MANAGEMENT AND SAFETY

11.1 Introduction

The following sections define medical events, serious adverse events, and unanticipated events and the procedures that will be followed in the trial to reduce the risk of all such occurrences.

11.2 Definitions

Definitions are obtained from the “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events Office for Human Research Protections (OHRP)” [http://www.hhs.gov/ohrp/policy/AdvEvtGuid.htm]. The requirements and processes of the National Heart, Lung, and Blood Institute are also implemented.

11.2.1 Medical events and serious adverse events

An adverse event is defined as any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. Abnormal laboratory results will be considered adverse events if they are not refuted by a repeat test conducted to confirm the abnormality or if the abnormality is of a degree that requires active clinical management.

Medical events and symptoms will be collected and reported from the beginning of study-related procedures to the end of the study follow-up period for an individual participant. At each assessment visit, SNAP staff will specifically query participants for medical events using the Medical Events form (see Appendix 4). Information on adverse events may also be reported to study staff during intervention contacts, as well as through telephone calls and emails, and will be recorded on the study interim event form. Adverse events will be followed until resolution, stabilization, or until it is determined that the study participation is not the cause. If there are any positive responses on the Medical Events form, the form will be reviewed by the appropriate study personnel (e.g., safety officer, study clinician, etc) to determine if a Serious Adverse Event Form should be completed.

Consistent with NHLBI guidelines and OHRP policy, serious adverse events (SAEs) are adverse events that meet any of the following criteria: fatal or life-threatening, poses an immediate risk of death, result in significant or persistent disability that lasted at least 1 month and changed your life, requires an overnight stay in the hospital but NOT the emergency room, result in a congenital anomaly/birth defect, or are important medical events that investigators judge to represent significant hazards or harm to research subjects. Any adverse event that meets any of these criteria (e.g. results in hospitalization) will be documented and reported as a serious adverse event. The serious adverse event form will be completed by staff or investigators with the help of the participant who can provide information about the event.
11.2.2 Unanticipated problems
An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria: 1) unexpected 2) related or possibly related to participation in the research; and 3) suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized. According to OHRP regulations, an incident, experience, or outcome that meets the three criteria for an unanticipated problem generally will warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others. Only a small subset of adverse events will be unanticipated problems.

11.3 Reporting of Serious Adverse Events and Unanticipated Problems
Selected serious adverse events will be reported to the Coordinating Center within 24 hours of knowledge of the event; these will include any deaths and serious adverse events that occurred on-site. The Coordinating Center will be responsible for timely reporting to the NIH, the DSMB, and other pertinent regulatory authorities. The Coordinating Center will provide reports of serious adverse events for review by the DSMB at their meetings.

If an adverse event that meets criteria for an unanticipated problem occurs at a SNAP site, the Principal Investigator of that site will promptly report the problem to their institution’s IRB, as required by OHRP and NHLBI policy. Any event/problem that is fatal, life threatening or otherwise serious AND unexpected, AND definitely, probably or possibly related to study participation, will be reported to NHLBI within 7 calendar days. OHRP will be notified within 30 days.

11.4 Potential Risks to Study Participants
11.4.1 Potential risks/adverse events due to study participation
SNAP presents low risk to study participants, given the young age of the study population and the nature of the interventions and study measurements. Participants may experience faintness or bruising from the collection of the blood sample, while infection at the site is possible but rare. Weight loss may result in increased fertility which could increase the likelihood of becoming pregnant. Increasing physical activity may result in joint discomfort, muscle soreness, exacerbation of pre-existing hernia or musculoskeletal injuries, exacerbation of exercise-induced asthma, and new-onset minor injuries including sprains and fractures. Participants may not lose weight or may gain weight. Cholecystitis may occur with weight loss. Transient increases in the risk of sudden death and acute myocardial infarction occurring during a bout of vigorous exercise have been observed, especially in previously sedentary individuals, but these events are expected to be rare in young adults of the age range included. Adverse events that may occur with weight loss and increased physical activity, including fractures, sprains, acute asthma exacerbation requiring emergency care, and gall bladder problems will be carefully monitored and reported.

Given the age and weight range of this population, the greatest concerns are that participants may engage in unsafe dietary practices, lose weight more quickly or to lower levels than recommended, or develop untoward psychological reactions. Previous studies by Stice and colleagues have shown that normal weight women, aged 18-29, who were placed on calorie restricted diets for 6 weeks and lost significant amounts of weight, had decreases in bulimic
symptoms relative to controls. Other weight gain preventions studies also indicate that participants in these programs increase their use of healthy weight control practices and decrease their use of unhealthy practices.

11.4.2 Anticipated adverse events in young adults
Adverse events, particularly serious events, not related to study participation are expected to be uncommon in this study of lifestyle intervention in generally health young adults. Nevertheless, young adults in this age range do experience acute health conditions and physical trauma that could result in serious adverse events, including disability, hospitalization and even death.

Common causes of serious adverse events and/or hospitalization in this age range include mental disorders, digestive system diseases, unintentional injuries, genitourinary diseases, respiratory diseases, musculoskeletal diseases, endocrine diseases, neoplasm/cancer, diseases of the heart, pregnancy and pregnancy-related complications, and infections. Births with congenital anomalies also occur although rates are rare. Other adverse events that occur in young adults include the development or worsening of eating disorders (e.g. bulimia nervosa), spontaneous and elective abortion, asthma exacerbation, and various injuries. The most common causes of death in this age range in the US are unintentional injuries (accidents, homicide), intentional injury (suicide), malignant neoplasm’s, diseases of the heart, congenital malformations, HIV disease, pregnancy/childbirth/puerperium, cerebrovascular diseases, diabetes mellitus, influenza/pneumonia, chronic lower respiratory diseases, chronic liver disease, and septicemia.

11.4.3 Minimization of risks
The SNAP protocol and interventions are designed to minimize the occurrence of any untoward effects. During the screening process, potential volunteers will be evaluated to determine whether it is safe for them to participate in the planned intervention. Medical problems that increase risk of study participation are assessed through questionnaires and telephone interviews, prior to randomization. The goal of these assessments is to detect conditions by history, such as recent major surgery, symptomatic conditions such as weight bearing pain, and asymptomatic conditions, such as eating disorders. To ensure medical readiness to begin physical activity, subjects will complete a physical activity readiness questionnaire (PAR-Q). The PAR-Q assesses for the following medical conditions: heart problems, chest pains, faintness or dizzy spells, high blood pressure, bone or joint problems such as arthritis that has been or could be aggravated by exercise, prescription medication use, and other medical reasons why exercise would not be advisable. Participants endorsing items 2-4 on the PAR-Q (frequent chest pains, or faintness or dizziness) will be excluded from the study. Participants endorsing other items (e.g., 5-7) will be required to obtain physician’s consent to participate. This screening protocol has been used successfully in our prior studies and 44% of overweight and obese participants required physician consent to participate. We anticipate lower rates in this trial due to recruitment of younger and primarily normal weight or moderate overweight individuals who likely have fewer comorbid conditions and medical usage.

All participants will be advised about safe weight loss or maintenance practices including dietary change and increasing physical activity at the initial group meeting. Participants will be advised to gradually increase their physical activity and to use walking as a primary form of activity and will be taught that the appropriate rate of weight loss is 1 to 2 pounds per week. In addition, we will carefully monitor changes in weight during our trial. We will collect information at each
assessment visit on hospitalizations for any psychiatric problem, including depression and eating disorders, and provide these data to the DSMB. We will track weight changes (using assessment data for controls and all weight data for intervention participants) and identify any individual who loses more than 20% of their body weight, has a BMI of 18.5 kg/m² or below at any point during the program, or loses more than 15 pounds in any month during the trial. We will meet individually with these participants within 2 weeks, discuss our concerns with them, and make referrals if appropriate. We will also arrange to see these participants again 1 month later. If there is no improvement in weight status, the participant will be unable to continue to participate in the interventions. However, we will continue to follow these individuals for outcome assessments.

Blood pressure will be measured at each clinic visit. We will use the JNC guidelines and inform any participant with Stage 1 hypertension (blood pressures of 140-159/90-99 mmHg) to be evaluated by their physician within 3 months; those with Stage 2 hypertension (blood pressures of 160-179/100-109 mmHg) to be evaluated by their physician with 1 month. If blood pressures >180/110 mmHg, participants will be advised to see their physician within 1 week or evaluated immediately depending on clinical situation and complications, based on a review conducted by a study clinician. We will also identify any participants with heart rate > 110 bpm. These participants will be advised to see their physician within 1 month. All information about blood pressure and heart rate levels will be conveyed to participants verbally at the time of these measurements and in writing immediately after the visit with the above recommendations regarding contacting their physician. We will caution participants with elevated blood pressures about doing physical activity until they are able to have their blood pressures re-checked.

Fasting glucose and lipid values will be obtained only at baseline, and month 24. The results of these tests will be available within about 2 weeks of completing the blood work and will be conveyed to participants in written format. If LDL-cholesterol levels exceed 160 mg/dl or triglycerides exceed 500 mg/dl, participants will be asked to contact their physician. If glucose levels are <60 or ≥126 mg/dl, participants will be informed of these values and given the option of having them repeated at our clinic or seeing their physician. All abnormal blood pressure, glucose and lipid values will be reviewed by a clinician at the local center before sending the results to the participant.

Table 11.4.3.1 summarizes the SNAP alert values and the action required.
Table 11.4.3.1 Alert Values and Action Required

<table>
<thead>
<tr>
<th>ALERT</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Participants will be given the JNC VII blood pressure recommendations and follow-up guidelines at each visit. Clinic staff will inform the participant at time of measurement.</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>Participant advised to see a health care provider within 3 months</td>
</tr>
<tr>
<td>SBP 140-159 OR DBP 90-99 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td>SBP 160-179 OR DBP 100-109 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Stage 3 hypertension</td>
<td>Participant advised to see a health care provider within 1 week or immediately</td>
</tr>
<tr>
<td>SBP ≥ 180 OR DBP ≥ 110 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Heart rate &gt; 110 bpm</td>
<td>Clinic staff will inform the participant at time of measurement. Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td>Lab Values</td>
<td>Notify participants within 1 month of receiving lab values</td>
</tr>
<tr>
<td>LDL &gt; 160</td>
<td>Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
</tr>
<tr>
<td>TG ≥ 500 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Glucose &lt; 60 or ≥126 mg/dl</td>
<td>Participant given the option of going to their physician or re-checking in clinic; if abnormal on re-check, inform participant to see a health care provider within 1 month</td>
</tr>
<tr>
<td>Excessive weight loss</td>
<td>Meet in person to counsel participant, within 2 weeks. If participant remains below 18.5 kg/m² or continues to lose more weight, intervention activities will stop.</td>
</tr>
<tr>
<td>BMI ≤ 18.5 kg/m² or greater than 20% weight loss from baseline weight or loses more than 15 lbs within any month</td>
<td></td>
</tr>
<tr>
<td>Eating Disorder/Eating habits</td>
<td>If a participant develops Bulimia Nervosa during the course of the trial (i.e., they meet full diagnostic criteria for BN at any follow-up assessment), we will temporarily discontinue treatment until the participant is healthy. A qualified staff member will meet with the participant individually and counsel them to seek professional treatment, and a list of referrals and/or a community resource guide will be provided. The participant will need medical consent/clearance before resuming treatment in the current study.</td>
</tr>
</tbody>
</table>
We will also monitor any major musculoskeletal problems that develop during the intervention (e.g. broken bones) and determine whether these appear related to our intervention. Participants who develop musculoskeletal problems or other health problems that may affect the safety of the intervention will be instructed to stop exercising until the problem resolves and their physician approves the resumption of physical activity.

Since young adults are targeted in this trial, we expect that pregnancies will occur. We will stop all intervention activities during the pregnancy. However, at 6 months post-partum, we will encourage participants to return to the intervention and the assessments for this trial.

All participants will be given access to the study website using a unique username and password to protect confidentiality. Participants in the intervention groups (Large and Small Changes) will be asked to submit their weight through the password protected website or by registering their cell phone number on the website and submitting their weight via SMS text from their cell phone.

All key personnel will have attended the required courses on human subject protection and HIPAA regulations, and certificates of IRB completion are on file with the Miriam Hospital, the University of North Carolina, and Wake Forest University Health Sciences. Subjects will be recruited through newspaper advertisements, community organizations, worksites, postings to Internet sites and mass mailings. Participants who are eligible based on initial telephone screening will be invited to attend an orientation session during which all aspects of this study will be described in detail and individuals will be given an opportunity to ask specific questions of the investigators regarding this study. Following this orientation session, individuals expressing a desire to participate in this study will be asked to sign an Informed Consent Form which has been approved by the Institutional Review Boards at the Miriam Hospital and the University of North Carolina, and Wake Forest University Health Sciences. In addition we will comply with all HIPPA regulations.

12. INTERIM ANALYSES AND MONITORING
Regular progress reports will be provided to the Data and Safety Monitoring Board (DSMB). These will describe recruitment, adherence, conduct, safety, study measures and outcomes.

We do not propose to conduct formal interim statistical tests on efficacy. Our reasoning for this is that this trial is not masked, the proposed interventions are based on publicly available research, and there is not a strong ethical imperative to terminate one or more arms before the planned end of the trial on the basis of efficacy. Even if differences between arms occur early, continued study of all three arms allows for better assessment of long-term effects and perhaps a greater chance to detect differences between the active intervention arms.

We also do not see a strong rationale to develop specific rules for stopping the trial early for futility. The time courses of intervention effects, in relation to the Control group, may be difficult to project from interim data. We are prepared, if requested by the DSMB at any point, to calculate interim statistical power for its review. Projections of interim power can be made under several scenarios for future data, including assumptions that current trends continue or that the future data reflect the relative effects used in the design of the trial.
Safety reports will tally adverse events by intervention assignment and postulated relationship to the trial interventions; event rates will be reported per person year of follow-up. The DSMB will consider, midway through the trial, whether there exists a strong rationale for developing a proposal to provide for post-trial follow-up of participants. If so, a plan for early unmasking of the clinical center Principal Investigators will be developed to enable the preparation of this proposal. It will be necessary to reconsent participants for any extensions of planned follow-up.

13. ANALYSIS PLANS
For the primary analysis, SNAP will analyze participants according to their randomization assignment and include evaluable data from all visits. Supporting analyses will examine relationships between markers of intervention adherence and outcomes. Inferences will be 2-tailed. Our primary analyses will include only clinic site as a covariate. The impact of any chance imbalances in baseline characteristics in the participants randomly assigned to the three intervention conditions will be explored. Secondary analyses will assess the impact of any marked imbalances using covariate-adjustments.

13.1 Primary Hypotheses
The primary outcome measure, changes in weight from baseline over time, will be assessed at 4-, 12-, 24-, 36- (80% of cohort), and 48-months (20% of cohort). All measured weights will be included in the analyses, except any that may have occurred during a pregnancy or within 6 months post-pregnancy. It will be contrasted among intervention groups using generalized linear models fitted by maximum likelihood with an unstructured covariance matrix. Estimated mean differences for each pairwise comparison will be developed using linear contrasts and assessed with Wald statistics, using Bonferroni adjustment to control total Type I error to be 0.05 across the three comparisons. In the primary analysis, missing weight measurements will be assumed missing at random, however the following supporting analyses will be conducted. Differences in baseline characteristics between participants with complete versus incomplete follow-up will be described. To gauge the sensitivity of our results to any changes in height, we will conduct supporting analyses of changes in BMI.

13.2 Secondary Hypotheses
To address secondary aim 1, pair wise differences in the secondary outcome measure, weight gain (yes/no), will be assessed using generalized estimating equation (GEE) methods, which control for the intra-subject correlations in this dichotomous measure over time. The three pairwise comparisons will be tested with the significance level equally distributed to control the overall Type I error to be 0.05. Wald statistics will be used to test the relative difference in the parameter $I_i$ between intervention assignments in the model: \[
\text{Logit}(p_{gijk}) = \beta_0 + \beta_C C_g + \beta_I I_i + \beta_T T_j + P_k \]
where $C$ denotes the covariates (clinical centers identified by “g”), $I$ is a marker for the intervention “i”, $T$ is a maker for time (i.e. the visit “j”) and $P$ is marker for individual participant “k”. In separate supporting analyses, Markov models will be fitted to parameterize the transition rates among the three states of no weight gain, weight gain, and missing data. Pairwise differences in changes of behavioral and psychosocial measures will be made using generalized linear models and GEE, as above.
Secondary aim 2 is an assessment of pairwise differences among intervention arms at 24-months post-randomization. This will be done using linear constraints and Wald tests to define and test differences at this time point within the framework of the general linear models used in aim 1. Two-sided tests will be used with Bonferroni-adjustment to maintain overall Type I error for this secondary aim at 0.05.

Generalized linear models will be used for aims 3 and 4, in a manner similar to that used for assessing weight changes. The effects on outcomes of demographic and psychological measures will be examined (aim 5) by including initial BMI, ethnicity, age, scores on the eating inventory, and intervention preference. Significant interaction effects will be plotted to illustrate the moderating effects, further assisting the interpretation for whom and under what circumstances the intervention has different effects. The active interventions tested for this trial aims to produce changes in diet, physical activity, restraint, and self-regulatory behaviors. Secondary aim 6 examines potential mediators of the effect of intervention, i.e., whether or not changes in diet, physical activity, restraint, and self-regulatory behaviors are in the causal pathway between the intervention and outcomes. For the primary outcome of weight gain, a continuous measure, a series of three linear regression models will be fit to test for mediators following the procedures introduced by Baron and Kenny. The Sobel’s test will be used to test the significance of the indirect effect. The joint effects of multiple mediators will also be tested. For the secondary outcome of weight gain (yes/no), we will run logistic regression models to assess mediational effects. Aim 7 will be addressed with proportional hazards regression to assess the distributions of incidence times for obesity and with GEE methods to compare the proportion of obese participants over time among the intervention groups.

Supporting analyses will be used to explore other ways to summarize the longitudinal dichotomous outcome of weight gain by using survival analyses to explore the distribution of times until the first weight gain and Poisson regression to model the proportion of examination times when weight gain was observed.

We pre-specify three planned subgroup comparisons. We will assess, using tests of interaction, whether the relative efficacy of the intervention varies according to baseline BMI (<25 kg/m² versus ≥25 kg/m²), age (<25 years versus ≥25 years), and gender.

13.3 Supporting Analyses
The fidelity of intervention delivery within the two Clinical Sites will be assessed by comparing measures of adherence and weight control. Adverse events will be tallied by intervention assignment and for important clinical subgroups.

The EARLY network of weight gain prevention trials is defining a secondary analysis that will be performed in a uniform fashion across all studies. SNAP will perform this analysis on its data and report findings to the EARLY network.

14. DATA DISTRIBUTION AND SHARING
Participant consent will specifically allow data sharing among SNAP sites including the Coordinating Center and investigators and subsequent distribution of de-identified data. Study databases will be distributed to Clinical Site principal investigators after the trial’s end to
facilitate continued data exploration. Data sharing within the EARLY clinical trial network may also occur.

NIH policy (issued 2003) states: “We believe that data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health. The NIH expects and supports the timely release and sharing of final research data from NIH-supported studies for use by other researchers.” SNAP data will be owned jointly by the individual clinical centers, NIH, and the coordinating center. The SNAP investigators will make no use of study data, nor disclose them to any other parties, except as specified in the Protocol or Manual of Operations or approved by the study group. The Coordinating Center will provide edited relevant data to approved ancillary study principal investigators. Only data approved by the study group will be released. The timing of data release must also be approved by the study group.

If ancillary studies are added to SNAP, their principal investigators will be responsible for providing the Coordinating Center edited ancillary study-specific data within 1 year of their termination. Ownership of such data is shared by the ancillary study Principal Investigator and the Coordinating Center. When the Coordinating Center ceases to function as an analytic resource to SNAP, it will release a fully documented copy of all data to each Clinical Site and the NIH. Decisions regarding disclosure of data to other parties, such as pharmaceutical companies or the FDA, shall be determined by the study group. Confidentiality of individual participants will be maintained with all releases of data.”

Within two years of when data collection ends, the final SNAP study analytical database will be processed according to HIPAA rules for public data sharing. We will de-identify participant data, using standard processes that include removal of identifiers, translation of dates and ages to delta time values, and assignment of random study identifiers. This will yield a series of de-identified data files, which will be available in a standard formats that are readable across a variety of applications and operating systems. The following documentation will be provided: data dictionary, data code book, valid variable ranges, protocol, procedure and operational manuals, and electronic versions of forms. Data sharing files and documentation will be provided by the Principal Investigator through an industry acceptable medium. Any stored laboratory samples, including DNA, will be transferred to the NIH repository two years after the end of the study.

The SNAP website will serve as a central distribution point for publicly available content. The site will contain recruitment materials and study brochures, community education materials, links to online materials, and contact information. Content management tools can be used to make as much of the content database driven as possible in order to facilitate support. File upload systems will allow approved staff to manipulate website content and allow regular review and updates.

15. TIMELINE
The planned timeline for SNAP consists of three phases: start-up, recruitment/follow-up, and analysis/close-out. The sample size and power estimates for this trial that were presented above
are based on the expectation that Cohort 1 (N = 120) will have 48 months of data, Cohorts 2, 3 and 4 will have 36 months of data and Cohort 5 will have 24 months of data.

16. ORGANIZATION
The relatively small size and the experience of its investigators allow SNAP to operate with a streamlined organization and few committees. The Steering Committee will be the primary governing body for the study, with each Principal Investigator accorded one vote. The Intervention Committee will oversee the design and implementation of the interventions. The Quality Control Committee will oversee the design and implementation of the data collection system. A Data Safety Monitoring Board (DSMB) will be convened by NHLBI and will be responsible for overseeing the safety and conduct of this trial.
16. BIBLIOGRAPHY


42. Gorin A, Pinto A, Smith-West D, Niemeier HM, Fava JL, Wing RR. Losing weight because you want to rather than because you feel you have to: Motivational predictors of weight loss outcomes. Paper presented at: The Obesity Society 2007 Annual Scientific Meeting, 2008; Phoenix, AZ.


Summary of Protocol Changes (other than editorial corrections):
October 11, 2011 Revision

**Table 9.1.1 Data Collection Schedule. Amended.** This table was amended to include collection of armband data during the 12 month follow-up visit.

**9.1.3 Behavioral and cognitive measures. Added.** The objective assessment of physical activity (the Sense-Wear Pro Armband) will be completed at month 12, in addition to month 4 and month 24.
Summary of Protocol Changes (other than editorial corrections):
June 20, 2011 Revision

3.2 Specific Aims. Added. Added Secondary Aim 7: To compare the incidence rates of obesity ((BMI > 30 kg/m²) and the proportions of participant who meet this criteria for obesity over time among the three groups.

4. Study Population. Amended. Clarified that individuals with type 2 diabetes would be allowed to participate, with permission from their health care provider.

4. Study Population. Added. Individuals with pulse > 110 or triglycerides ≥ 500 mg/dl are eligible for participation with permission from their primary care physician. Individuals reporting heart disease, heart problems, or participants who report being prescribed drugs for blood pressure or a major heart condition are eligible with permission from their primary care physician. Individuals with health problems that may limit their physical activity may participate, with permission from their health care provider.

4. Study Population. Amended. Individuals with type 1 diabetes or type 2 diabetes treated with insulin or oral medications that may cause hypoglycemia will be excluded from participating in the SNAP trial.

4. Study Population. Amended. Individuals reporting a heart attack or stroke will be excluded. Previously this stated heart condition.

4. Study Population. Deleted. Deleted reference to individuals reporting a diagnosis of acromegaly or Cushing’s syndrome. While these individuals may still be excluded from participation, given the study population, all potential participants will not be asked directly if they have these diseases.

4. Study Population. Added. Individuals who report that they are trying to gain weight, currently using steroids for muscle mass or weight gain will be excluded from participation.

4. Study Population. Amended. Individuals with residence or place of work further than 30 miles from the intervention site will be excluded. Previously, this had stated residence or place of work must be within 50 miles.

4. Study Population. Amended. Individuals with perceived inability to attend the intervention and assessment visits will be excluded. Previously, this had stated perceived inability to attend the 2 year data collection visit.

4. Study Population. Added. Individuals who report bone problems that may limit exercise will be required to obtain permission from their physician.

5. Recruitment and Screening. Amended. Participant will be recruited in cohorts of approximately 45 to 60 (15 to 20 randomized to each group).
5. Recruitment and Screening. Amended. At the first screening visit, the Center for Epidemiologic Studies Depression (CES-D) Scale will be administered by study staff.

5. Recruitment and Screening. Amended. Clarified administration of the armband. The goal will be to have participants record their activity for at least 8 hours per day on 4 of the 7 days (including 1 weekday and 1 weekend day). This will not be required for eligibility.

5. Recruitment and Screening. Amended. At the second screening visit, participants will be given information about how to complete self-report questionnaires about their medical history, in addition to their health habits. At the second screening visit, staff will administer the Exercise Habits (Paffenbarger) Form.

5. Recruitment and Screening. Amended. Participants who seem appropriate for the trial will be called during the two weeks prior to randomization to ensure they are still eligible and not pregnant. After this, they will be randomly assigned to one of the three treatment groups.

6. Randomization. Deleted. The system provides reports of expected follow-up sequences and missed appointments.

6. Randomization. Deleted. The randomization checklist does not require the participants to meet the requirements for the armband or reporting that they will be available through a 2-year follow-up.

7. Retention. Added. Individuals in their first trimester will be seen for assessment visits, but will not participate in the intervention because it may be contraindicated.

8.2.1 Contact Schedules. Amended. The intervention meetings will occur over approximately 16 weeks.

Table 9.1.1 Data Collection Schedule. Amended. This table was amended to include current data collection measures and scheduling changes. Several of these changes were made so that the SNAP study would be consistent with the EARLY studies. These changes include: adding collection of weight history at baseline; adding collection of information about their neighborhood and environment at baseline, 4 month, 12 month and annually thereafter; adding collection of medical events at 4 month, 12 month and annually thereafter; adding collection of contact information at baseline, 4 month, 12 month and annually thereafter; and adding collection of treatment preference, satisfaction and post-treatment feedback at 4 month, 12 month and annually thereafter (previously just collected at baseline and month 48).

9.1.2 Anthropometric measures. Amended. If the difference between the first two measures differs by more than 0.2 kg (weight) or 0.5 cm (height), a third measurement will be taken. This change was made for consistency with the EARLY studies.

9.1.2 Anthropometric measures. Amended. For measurements of body composition using the BodPod, participants will be asked to refrain from alcohol for at least 12 hours and to refrain from strenuous exercise or sauna for 8 hours prior to these measures.
9.1.3 Behavioral and cognitive measures. Amended. Participants will be instructed to wear the armband devise for at least 8 hours per day. This was previously 10 hours per day.

9.1.3 Behavioral and cognitive measures. Deleted. If the device is not worn for at least this amount of time, the participants will be instructed to wear the device again during another full week. If at baseline, the data remain incomplete on this second attempt, the individual will not be randomized; if at later assessments, the data on the second attempt remain incomplete, the available data will be used.

9.1.3 Behavioral and cognitive measures. Added. Instructions about weight history questionnaire: Weight History. Participants will complete a questionnaire reporting their weight history, including information about why they joined the program, highest and lowest weight, and weight at key age intervals.

9.1.3 Behavioral and cognitive measures. Amended. Participants will be asked about their use of specific weight management strategies over the past 4 months. This was asked about the previous 6 months.

9.1.3 Behavioral and cognitive measures. Added. Instructions about neighborhood/environment questionnaire: Neighborhood, environment. A questionnaire will be administered at each assessment that asks about the neighborhood and environment and the facilities that are available.

9.1.4 Clinical measures. Added. Instructions about collection of medical events: Medical events and symptoms will be collected at each assessment visit after baseline, using a standard form that is administered by study staff. Any positive responses will be reviewed by appropriate study personnel to determine if an SAE form is required.

9.1.5 Psychological assessments. Amended. The CES-D will be collected at all assessment visits (previously this was specified to be collected just at the baseline visit).

9.1.6 Supporting measures. Added. Instruction about contact information collection: Contact information will be collected at baseline and each assessment visit in order to assist clinic staff with retention.

9.1.6 Supporting measures. Added. The post-treatment process evaluation will include describing the perception of the program.


10.3 Website and Security. Added. Added clarification about website security.

10.4 Quality Control. Amended. Uploads to the website will also include data from the Food Frequency, Bod Pod, Intervention and Accelerometry data.

11.2.1 Medical events and serious adverse events. Added. If there are any positive responses on the Medical Events form, the form will be reviewed by the appropriate study personnel (e.g., safety officer, study clinician, etc) to determine if a Serious Adverse Event form should be completed.

11.2.1 Medical events and serious adverse events. Amended. SAE definitions modified for consistency with NHLBI guidelines and OHRP policy: Serious adverse events (SAEs) are adverse events that meet any of the following criteria: fatal or life-threatening, poses an immediate risk of death, result in significant or persistent disability that lasted at least 1 month and changed your life, requires an overnight stay in the hospital but NOT the emergency room, result in a congenital anomaly/birth defect, or are important medical events that investigators judge to represent significant hazards or harm to research subjects. Any adverse event that meets any of these criteria (e.g. results in hospitalization) will be documented and reported as a serious adverse event. The serious adverse event form will be completed by staff or investigators with the help of the participant who can provide information about the event.

11.3 Reporting of Serious Adverse Events and Unanticipated Problems. Amended. SAE reporting techniques modified for consistency with NHLBI guidelines and OHRP policy: If an adverse event that meets criteria for an unanticipated problem occurs at a SNAP site, the Principal Investigator of that site will promptly report the problem to their institution’s IRB, as required by OHRP and NHLBI policy. Any event/problem that is fatal, life threatening or otherwise serious AND unexpected, AND definitely, probably or possibly related to study participation, will be reported to NHLBI within 7 calendar days. OHRP will be notified within 30 days.

11.4.1 Potential risks/adverse events due to study participation. Added. Added weight loss as an expected adverse event: Weight loss may result in increased fertility which could increase the likelihood of becoming pregnant.

11.4.3 Minimization of risks. Amended. Amended alerts and response for consistency with the EARLY studies: Blood pressure will be measured at each clinic visit. We will use the JNC guidelines and inform any participant with Stage 1 hypertension (blood pressures of 140-159/90-99 mmHg) to be evaluated by their physician within 3 months; those with Stage 2 hypertension (blood pressures of 160-179/100-109 mmHg) to be evaluated by their physician with 1 month. If blood pressures >180/110 mmHg, participants will be advised to see their physician within 1 week or evaluated immediately depending on clinical situation and complications, based on a review conducted by a study clinician. We will also identify any participants with heart rate >110 bpm. These participants will be advised to see their physician within 1 month. All information about blood pressure and heart rate levels will be conveyed to participants verbally at the time of these measurements and in writing immediately after the visit with the above recommendations regarding contacting their physician. All abnormal blood pressure, glucose and lipid values will be reviewed by a clinician at the local center before sending the results to the participant.
**Table 11.4.3.1 Alert Values and Action Required, Amended.** Table 11.4.3.1 was amended for consistency for the EARLY studies. The updated table is below:

<table>
<thead>
<tr>
<th>ALERT</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Pressure</strong></td>
<td>Participants will be given the JNC VII blood pressure recommendations and follow-up guidelines at each visit. Clinic staff will inform the participant at time of measurement.</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>Participant advised to see a health care provider within 3 months</td>
</tr>
<tr>
<td>SBP 140-159 OR DBP 90-99 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td>SBP 160-179 OR DBP 100-109 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Stage 3 hypertension</td>
<td>Participant advised to see a health care provider within 1 week or immediately</td>
</tr>
<tr>
<td>SBP ≥ 180 OR DBP ≥ 110 mm/Hg</td>
<td></td>
</tr>
<tr>
<td>Heart rate &gt; 110 bpm</td>
<td>Clinic staff will inform the participant at time of measurement. Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td><strong>Lab Values</strong></td>
<td>Notify participants within 1 month of receiving lab values</td>
</tr>
<tr>
<td>LDL &gt; 160</td>
<td>Participant advised to see a health care provider within 1 month</td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
</tr>
<tr>
<td>TG ≥ 500 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Glucose &lt; 60 or ≥ 126 mg/dl</td>
<td>Participant given the option of going to their physician or re-checking in clinic; if abnormal on re-check, inform participant to see a health care provider within 1 month</td>
</tr>
<tr>
<td><strong>Excessive weight loss</strong></td>
<td>Meet in person to counsel participant, within 2 weeks. If participant remains below 18.5 kg/m² or continues to lose more weight, intervention activities will stop.</td>
</tr>
<tr>
<td>BMI ≤ 18.5 kg/m² or greater than 20%</td>
<td></td>
</tr>
<tr>
<td>weight loss from baseline weight or loses more than 15 lbs within any month</td>
<td></td>
</tr>
<tr>
<td><strong>Eating Disorder/Eating habits</strong></td>
<td>If a participant develops Bulimia Nervosa during the course of the trial (i.e., they meet full diagnostic criteria for BN at any follow-up assessment), we will temporarily discontinue treatment until the participant is healthy. A qualified staff member will meet with the participant individually and counsel them to seek professional treatment, and a list of referrals and/or a community resource guide will be provided. The participant will need medical consent/clearance before resuming treatment in the current study.</td>
</tr>
</tbody>
</table>
11.4.3 Minimization of risks. Amended. Confidentiality criteria set for the intervention website were amended: All participants will be given access to the study website using a unique username and password to protect confidentiality. Participants in the intervention groups (Large and Small Changes) will be asked to submit their weight through the password protected website or by registering their cell phone number on the website and submitting their weight via SMS text from their cell phone.

11.4.3 Minimization of risks. Amended. Recruitment methods were amended: Subjects will be recruited through newspaper advertisements, community organizations, worksites, postings to Internet sites and mass mailings.

13.2. Secondary Hypotheses. Added. Aim 7 will be addressed with proportional hazards regression to assess the distributions of incidence times for obesity and with GEE methods to compare the proportion of obese participants over time among the intervention groups.

16. Bibliography. Amended. The bibliography was amended as necessary for the changes above.
Summary of Protocol Changes (other than editorial corrections):  
June 11, 2010 Revision

1. Executive Summary. Added. SNAP is member of the Early Adult Reduction in Weight Through Lifestyle Interventions (EARLY) consortium of clinical trials funded by the National Heart, Lung, and Blood Institute.

Table 9.1.1 Data Collection Schedule. Amended. Corrected table to indicate that blood collection will occur at 24 month visit.

9.1.2 Behavioral and cognitive measures. Added. More complete instructions about armband use were added. Participants will be instructed to wear the device during all waking hours (except swimming and showering) for a full week; monitoring for at least 10 hours per day for at least 4 days in the week (including at least one weekday and one weekend day) will be considered adequate for analysis. If the device is not worn for at least this amount of time, the participants will be instructed to wear the device again during another full week. If at baseline, the data remain incomplete on this second attempt, the individual will not be randomized; if at later assessments, the data on the second attempt remain incomplete, the available data will be used.

9.1.7 Measures of intervention fidelity. Amended. Instructions regarding the written intervention fidelity form were corrected. The reviewer will listen to the session tape and complete a written form indicating whether it was a small or large change intervention session and indicate the basic message provided to participants about the diet, physical activity, and the weight change goal of the intervention.

11.2.1 Adverse events and serious adverse events. Added. The serious adverse event form will be completed by staff or investigators with the help of the participant who can provide information about the event.

11.4.3 Minimization or risks. Added. We will continue to follow individuals who set off a weight alert, but show no improvement in weight status, for outcome assessments.

11.4.3 Minimization or risks. Deleted. Consistent with the EARLY studies, we will not identify participant with blood pressures < 90 mmHg.

11.4.3 Minimization or risks. Amended. Abnormal blood pressure, glucose and lipid values will be reviewed by a clinician at the local center before sending these results to the participant. Results will not be shared with the participant’s physician directly by the SNAP study.

13.1 Primary Hypotheses. Added. All measured weights will be included in the analyses, except any that may have occurred during a pregnancy or within 6 months post-pregnancy.

13.3 Supporting Analyses. Added. The EARLY network of weight gain prevention trials is defining a secondary analysis that will be performed in a uniform fashion across all studies. SNAP will perform this analysis on its data and report findings to the EARLY network.
14. Data Distribution and Sharing. Added. Data sharing within the EARLY clinical trial network may also occur.
Summary of Protocol Changes (other than editorial corrections):
March 18, 2010 Revision

1. Executive Summary. Amended. Secondary Aim 1, we will compare the three groups on the proportion of participants in the three groups who gain less than 1 pound over the planned follow-up.

1. Executive Summary. Added. Secondary Aim 2, we will compare the three groups on the mean difference in weight gain from baseline to 24-month follow-up.

Throughout. Amended. Control condition referred to as control group; self-guided behavioral changes.

4. Study Population. Amended. Individuals with untreated hypertension, hyperlipidemia, or diabetes are eligible for participation with permission from their primary care physician. Participants who do not currently have a health care provider will be given a list of local providers.

4. Study Population. Amended. Individuals with residence, or place of work, further than 50 miles from the intervention site will be excluded from participating in the SNAP trial.

5. Recruitment and Screening. Amended. Participants will be instructed to wear the SenseWear Pro Armbands for at least 10 hours per day on 4 of the 7 days (including 1 weekday and 1 weekend day).

5. Recruitment and Screening. Deleted. Screening Visit 2 will not be required to occur within 1 month of randomization.

5. Recruitment and Screening. Added. Baseline measure of body composition will occur at Screening Visit 2.

6. Randomization. Added. In order for a participant to be randomized, he/she must have signed the informed consent, be in the eligible BMI and age categories, not report any of the health problems described above for ineligibility, have physician permission to join the study if deemed necessary based on health parameters (see eligibility), complete blood pressure and blood work for lipids, glucose, and insulin, complete the requirements for the SenseWear Pro arm band (worn at least 4 days, including 1 weekday and 1 weekend day, with 10 hours of reporting each day), successfully complete the behavioral interview, be available for the time/place that treatment is being conducted and report being available through a 2 year follow-up.

6. Randomization. Amended. Stratification by ethnicity for randomization purposes clarified (Non-Hispanic white versus other race/ethnic groups).

8.1. Control Condition. Amended. The control group will be given the message that by providing them with information about both approaches they can choose whichever approach they feel will work better for them.
8.1. **Control Condition, Amended.** The Control group description amended to indicate participants randomized to this arm will also be granted access to the study website to access the quarterly newsletters covering weight gain prevention topics and providing healthy recipes and exercise strategies.

8.3.1 **Self-regulation plus small behavior changes, Deleted.** The toolbox (provided by the study) will include a compilation of small changes that can be made to decrease intake and increase activity. The toolbox will also include a new pedometer and a reminder of their prior step goal, as well as copies of self-monitoring charts.

8.3.2 **Self-regulation plus large behavior changes group, Deleted.** This intervention group will be provided with a toolbox of supplies to use if they experience weight gain; their toolbox will include self-monitoring books, a meal plan to use for a 1200-1500 or 1500-1800 calorie diet and meal replacement products (such as Slim-Fast).

Table 9.1.1 **Data Collection Schedule, Amended.** Changes include: adding collection of body composition with impedance at baseline, 4 month, 12 month and annually thereafter; adding collection of body composition with BodPod (UNC only) at baseline, 4 month, 12 month and annually thereafter; and adding collection of sleep habits at baseline, 4 month, 12 month and annually thereafter.

9.1.2 **Anthropometric measures, Amended.** Waist circumference will be measured using a Gulik tape measure and following a standardized protocol. This previously stated that circumference would be measured at the midpoint between the highest point of the iliac crest and the lowest part of the costal margin in the mid axillary line.

9.1.2 **Anthropometric measures, Deleted.** We have completed these measures in prior studies and will use protocols developed for Look AHEAD.

9.1.2 **Anthropometric measures, Added.** Body composition. Both sites will complete measures of body composition with the RJL Systems Quantum II impedance machine. In addition, participants at UNC will also have body composition assessed with the BodPod. Participants will be asked to fast for 4 hours and to refrain from strenuous exercise for 24 hours prior to these measures.

9.1.3 **Behavioral and cognitive measures, Amended.** Diet will be assessed based on the consumption and the portion sizes consumed over the past month.

9.1.3 **Behavioral and cognitive measures, Amended.** Sedentary activity will be assessed using a self-report questionnaire, which asks respondents to indicate the number of hours they spend on a typical weekday and a typical weekend day doing a variety of sedentary activities. Previously it was specified that the PACE Adult Sedentary Behaviors Survey would be used.
9.1.3 Behavioral and cognitive measures. Added. Instructions about sleep habits questionnaire: Sleep Habits. A questionnaire will be administered at each assessment that asks about duration of sleep and problems encountered during sleep (e.g. snoring).

9.1.4 Clinical measures. Amended. In order to be consistent with the protocol for the EARLY studies, three blood pressure measurements will be taken. Blood collection samples will be collected at baseline and the 24 month visit.

9.1.7 Measures of intervention fidelity. Added.

11.4.3 Minimization of risks. Amended. Amended weight change alerts to include loss of more than 15 pounds in any month. This was changed from the previous alert for individuals who lose weight at a rate exceeding 2 pounds per week during the intervals between the planned clinic assessments.

11.4.3 Minimization of risks. Added. We will also identify any participants with blood pressures < 90 mmHg or heart rate > 110 bpm.

11.4.3 Minimization of risks. Added. All abnormal blood pressure, glucose and lipid values will be reviewed by a clinician at the local center before discussing these values with the participant or sending the results to the participant or their physician.

15. Timeline. Deleted. Removed Figure 1 with previous recruitment goals.
ANALYSIS PLANS
For the primary analysis, SNAP will analyze participants according to their randomization assignment and include evaluable data from all visits. Supporting analyses will examine relationships between markers of intervention adherence and outcomes. Inferences will be 2-tailed. Our primary analyses will include only clinic site as a covariate. The impact of any chance imbalances in baseline characteristics in the participants randomly assigned to the three intervention conditions will be explored. Secondary analyses will assess the impact of any marked imbalances using covariate-adjustments.

Specific Aims
The primary hypothesis of SNAP is that the magnitude of weight gain across an average planned follow-up of three years will differ among the three arms. Specific a priori hypotheses are that over an average of three years:
1. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus small behavior changes intervention compared to the control group;
2. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to the control group; and
3. The magnitude of weight gain will be lower in those who are randomly assigned to the self-regulation plus large behavior changes intervention compared to those assigned to the self-regulation plus small behavior changes intervention.

Secondary aims of SNAP are:
1. To compare the proportion of participants in the three groups (self-regulation plus small changes, self-regulation plus large changes, and control) who gain less than 1 pound over the planned follow-up of an average of three years;
2. To assess the mean differences in weight gain among intervention groups at 24 months post-randomization;
3. To compare the three groups on changes in behavior (e.g. diet, physical activity, abnormal eating behaviors, use of healthy and unhealthy weight control practices) and psychosocial measures (restraint, depression) over the average follow-up of three years;
4. To compare changes in cardiovascular disease risk factors (including blood pressure, lipids, insulin sensitivity, and waist circumference) across the three groups and examine the association of changes in cardiovascular disease risk factors with weight change and behavior changes;
5. To examine demographic and psychological variables that may moderate the effects of the interventions, including initial BMI, ethnicity, age, scores on the Eating Inventory, and treatment preference; and
6. To examine potential mediators of the effect of the interventions, including changes in diet, physical activity, restraint, and change in self-regulatory behaviors.

Analysis Plan Related to the Primary Hypotheses
The primary outcome measure, changes in weight from baseline over time, will be assessed at 4-, 12-, 24-, 36- (80% of cohort), and 48-months (20% of cohort). We have chosen this outcome, rather than other potential measures (e.g. percent weight change, BMI change, percent BMI change, or covariate-adjusted weight) in that this is the stated focus of our intervention. We feel that this choice will simplify the dissemination of findings from our trial.

All measured weights will be included in the analyses, except any that may have occurred during a pregnancy or within 6 months post-pregnancy. We have chosen not to plan for censoring weight data collected from participants following events that may have influence on weight (except as noted above for pregnancy); such events or incident conditions might include bariatric surgery, AIDS, cancer therapy, or traumatic injury, for example. Our rationale for this is that these events are likely to be rare in our cohort and are within the backdrop of usual care. We will plan supporting analyses that examine the influence of such events, if they occur.

Weight changes will be contrasted among intervention groups using generalized linear models fitted by maximum likelihood with an unstructured covariance matrix [Littell, 1996]. Estimated mean differences for each pairwise comparison will be developed using linear contrasts and assessed with Wald statistics, using Bonferroni adjustment to control total Type I error to be 0.05 across the three comparisons.

In the primary analysis, missing weight measurements will be assumed missing at random. The following supporting analyses will be conducted related to missing data. Differences in baseline characteristics (i.e. factors that may be associated with adherence to the interventions and weight changes, such as age, sex, education, ethnicity, baseline BMI, etc.) between participants with complete versus incomplete follow-up will be described to assess whether this provides evidence of differential follow-up. We will create propensity scores to examine how these factors may be associated with incomplete follow-up and conduct stratified analyses across subgroups formed by propensity score percentiles. If missing data appear to have the potential of influencing interpretations, we will also conduct multiple imputation using several different models for non-ignorable missingness. These will be used to assess the range of impact that missing data may exert on our results.

To gauge the sensitivity of our results to any changes in height, we will conduct supporting analyses of changes in BMI.

**Analysis Plans Related to Secondary Hypotheses**

To address Secondary Aim 1, pairwise differences in the secondary outcome measure, weight gain (yes/no), will be assessed using generalized estimating equation (GEE) methods, which control for the intra-subject correlations in this dichotomous measure over time. Our protocol defines weight gain as a measured increase in weight from baseline exceeding 1 pound.
The three pairwise comparisons will be tested with the significance level equally distributed to control the overall Type I error to be 0.05. Wald statistics will be used to test the relative difference in the parameter $I_i$ between intervention assignments in the model: \[ \text{Logit}(p_{gijk}) = \beta_0 + \beta_C C_g + \beta_I I_i + \beta_T T_j + P_k \] where $C$ denotes the covariates (clinical centers identified by “g”), $I$ is a marker for the intervention “i”, $T$ is a marker for time (i.e. the visit “j”) and $P$ is marker for individual participant “k”.

In separate supporting analyses, Markov models will be fitted to parameterize the transition rates among the three states of no weight gain, weight gain, and missing data.

The Secondary Aim 2 is an assessment of pairwise differences in mean weight changes from baseline among intervention arms at 24-months post-randomization. This will be done using linear contrasts and Wald tests to define and test differences at this time point within the framework of the general linear models used in aim 1. Two-sided tests will be used with Bonferroni-adjustment to maintain overall Type I error for this secondary aim at 0.05.

Generalized linear models will be used for Secondary Aims 3 and 4, in a manner similar to that used for assessing weight changes. The effects on outcomes of demographic and psychological measures will be examined (Secondary Aim 5) by including initial BMI, ethnicity, age, scores on the eating inventory, and intervention preference. Significant interaction effects will be plotted to illustrate the moderating effects, further assisting the interpretation for whom and under what circumstances the intervention has different effects. The active interventions tested for this trial aims to produce changes in diet, physical activity, restraint, and self-regulatory behaviors.

Secondary Aim 6 examines potential mediators of the effect of intervention, i.e., whether or not there is evidence that changes in diet, physical activity, restraint, and self-regulatory behaviors may be in the causal pathway between the intervention and outcomes. For the primary outcome of weight gain, a continuous measure, a series of three linear regression models will be fitted to test for mediators following the procedures introduced by Baron and Kenny [Baron, 1986]. The Sobel’s test will be used to test the significance of the indirect effect. The joint effects of multiple mediators will also be tested [MacKinnon, 2000]. For the secondary outcome of weight gain (yes/no), logistic regression models will be fitted to assess meditational effects [Huang, 2004].

Supporting analyses will be used to explore other ways to summarize the longitudinal dichotomous outcome of weight gain by using survival analyses to explore the distribution of times until the first weight gain and Poisson regression to model the proportion of examination times when weight gain was observed.

We pre-specify three planned subgroup comparisons. We will assess, using tests of interaction, whether the relative efficacy of the intervention varies according to baseline BMI (<25 kg/m$^2$ versus >25 kg/m$^2$), age (<25 years versus >25 years), and gender.

**Supporting Analyses**
The fidelity of intervention delivery within the two clinical sites will be assessed by comparing measures of adherence and weight control. Adverse events will be tallied by intervention assignment and for important clinical subgroups. We will report event rates per person years and use Poisson regression to compare rates of any commonly occurring events among intervention groups.

The EARLY network of weight gain prevention trials is defining a series of secondary analyses that will be performed in a uniform fashion across all studies. SNAP will participate in these analyses and report findings to the EARLY network.

References

