

SNAP (Study of Novel Approaches for Prevention) Protocol

Original: December 14, 2009

Revision 1: March 18, 2010

Revision 2: June 11, 2010

Revision 3: June 20, 2011

Revision 4: October 11, 2011

Revision 5: July 8, 2014

1. EXECUTIVE SUMMARY

Young adults, aged 20-35 years, experience the greatest rate of weight gain, averaging 1-2 lbs/yr.¹ Over time, this weight gain is associated with a worsening in cardiovascular disease risk factors and an increase in the prevalence of metabolic syndrome.^{2,3} 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.⁴ 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^{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.^{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,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.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.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,¹¹ 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),¹² 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 ($\text{BMI} > 30 \text{ kg/m}^2$) 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 $\geq 90\%$ 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,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)

	Year 1	Year 2	Year 3
Year 1	57.09	40.29	38.46
Year 2	40.29	124.99	78.23
Year 3	38.46	78.23	112.00

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 Bonferoni-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

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

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/from 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)¹⁶ 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 procedures for wearing the SenseWear Pro Armbands. 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.¹⁷⁻¹⁹ 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 Hunters²⁰ had a pregnancy; 11% of the women in POP²¹). 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-weighting 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

Time Frame	Meetings	Reporting Weight
Year 1		
Months 1-2	Weekly	None*
Months 3-4	Monthly	Weekly
Months 5-12	None	Monthly
Year 2	Annual 4 week refresher	Monthly
Year 3	Annual 4 week refresher	Monthly

*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.^{12, 13} Likewise face-to-face was more effective than Internet in preventing weight regain.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 Program²² and is being used currently in Look AHEAD^{22a}. 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.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 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;²³ changes in dietary pattern toward a more “prudent” dietary pattern and away from a Western pattern have also been associated with lower weight gains²⁴ 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 8.3.1: Treatment Components that Differ between the Two Intervention Groups

Key Intervention Concepts	Small Changes	Large Changes
Dietary changes recommended for maintaining weight (green zone)	Instructed to make one small change in diet every day	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
Physical activity changes recommended for maintaining weight (green zone)	Given pedometers and instructed to increase steps by 2000 steps per day over baseline levels and maintain this level	Instructed to exercise for 250 min/week (50 min/day on 5 days/week) throughout the entire program.
Self-monitoring of behavior changes	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.	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.
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)	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.	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.
What to do if exceed baseline or starting (red zone)	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.	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.

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.³³ 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 9.1.1 Data Collection Schedule

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

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.³⁴ 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)³⁵ 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.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.^{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.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.

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.^{43, 44}

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)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 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 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.

9.1.6 Supporting measures

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

Contact 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,⁴⁹ 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^{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 healthy 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

ALERT	ACTION
<i>Blood Pressure</i>	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.
Stage 1 hypertension SBP 140-159 OR DBP 90-99 mm/Hg	Participant advised to see a health care provider within 3 months
Stage 2 hypertension SBP 160-179 OR DBP 100-109 mm/Hg	Participant advised to see a health care provider within 1 month
Stage 3 hypertension SBP \geq 180 OR DBP \geq 110 mm/Hg	Participant advised to see a health care provider within 1 week or immediately
Heart rate > 110 bpm	Clinic staff will inform the participant at time of measurement. Participant advised to see a health care provider within 1 month
<i>Lab Values</i>	Notify participants within 1 month of receiving lab values
LDL > 160 Triglycerides TG \geq 500 mg/dl	Participant advised to see a health care provider within 1 month
Glucose < 60 or \geq 126 mg/dl	Participant given the option of going to their physician or re-checking check in clinic; if abnormal on re-check, inform participant to see a health care provider within 1 month
Excessive weight loss BMI \leq 18.5 kg/m ² or greater than 20% weight loss from baseline weight or loses more than 15 lbs within any month	Meet in person to counsel participant, within 2 weeks. If participant remains below 18.5 kg/m ² or continues to lose more weight, intervention activities will stop.
Eating Disorder/Eating habits	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.

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 re-consent 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.⁵⁵ 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 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. 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 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 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.⁵⁶ 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.⁵⁷ For the secondary outcome of weight gain (yes/no), we will run logistic regression models to assess mediational effects.⁵⁸ 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 ($<25 \text{ kg/m}^2$ versus $\geq 25 \text{ kg/m}^2$), 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 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.

17. SNAP extension

The primary aim of the SNAP study, described above, was to determine if either or both of the self-regulation interventions would decrease weight gain over an average of 3 years of follow-up (with some participants reaching 2, 3 or 4 years of follow-up depending on when they initially entered the trial). The SNAP study extension (SNAP- E) will extend SNAP through 6 years of follow-up. Only participants who have previously been enrolled in SNAP will be able to participate in SNAP-E. SNAP-E will be described to these participants either in person or via phone and all participants will be asked to sign an Addendum to the Original Consent to continue to participate in SNAP-E. The procedures used in SNAP-E are continuations of those that have been done in SNAP.

In SNAP-E most data and intervention will be conducted on-line. Participants will be given a Smart-Scale which enables them to weigh themselves at home and transmits their weight data to us. In addition, at 6 month intervals, they will be asked to complete several on-line questionnaires (which they have been doing in SNAP) and to transmit a weight to us using the Smart-Scale. In addition, those participants who were randomly assigned to the intervention groups of SNAP will continue to be offered two refresher courses each year. The refreshers will be primarily conducted on-line, but optional face-to-face meeting may be available at some refreshers. When each participant reaches Year 6 (6 years after they initially entered SNAP) they will be asked to attend a face-to-face assessment session. All measures conducted in SNAP will be completed again at this visit (including blood work, objective measure of physical activity via arm band, body composition measure via impedance). Participants will be sent a letter providing them with their own data from this visit as has been done throughout SNAP. Participants in SNAP-E will be provided with a \$50 honorarium for each 6 month on-line assessment and \$150 for attending the face-to-face assessment at Year 6.

16. BIBLIOGRAPHY

1. Williamson DF, Kahn HS, Remington PL, Anda RF. The 10-year incidence of overweight and major weight gain in US adults. *Arch Intern Med.* 1990 1990;150:665-672.
2. Truesdale KP, Stevens J, Lewis CE, Schreiner PJ, Loria CM, Cai J. Changes in risk factors for cardiovascular disease by baseline weight status in young adults who maintain or gain weight over 15 years: the CARDIA study. *Int J Obes.* Sep 2006;30(9):1397-1407.
3. Norman JE, Bild D, Lewis CE, Liu K, Smith-West D. The impact of weight change on cardiovascular disease risk factors in young black and white adults: the CARDIA study. *Int J Obes.* 2003;27:369-376.
4. Lloyd-Jones DM, Leip EP, Larson MG, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation.* Feb 14 2006;113(6):791-798.
5. Daviglius ML, Stamler J, Pirzada A, et al. Favorable cardiovascular risk profile in young women and long-term risk of cardiovascular and all-cause mortality. *JAMA.* Oct 6 2004;292(13):1588-1592.
6. Stamler J, Stamler R, Neaton JD, et al. Low risk-factor profile and long-term cardiovascular and noncardiovascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women. *JAMA.* Dec 1 1999;282(21):2012-2018.
7. Daviglius ML, Liu K, Pirzada A, et al. Cardiovascular risk profile earlier in life and Medicare costs in the last year of life. *Arch Intern Med.* May 9 2005;165(9):1028-1034.
8. Daviglius ML, Liu K, Pirzada A, et al. Favorable cardiovascular risk profile in middle age and health-related quality of life in older age. *Arch Intern Med.* Nov 10 2003;163(20):2460-2468.
9. Wing RR, Tate DF, Gorin AA, Raynor HA, Fava JL. A self-regulation program for maintenance of weight loss. *N Engl J Med.* Oct 12 2006;355(15):1563-1571.
10. Linde JA, Jeffery RW, French SA, Pronk NP, Boyle RG. Self-weighing in weight gain prevention and weight loss trials. *Ann Behav Med.* Dec 2005;30(3):210-216.
11. Hill JO, Wyatt HR, Reed GW, Peters JC. Obesity and the environment: Where do we go from here? *Science.* 2003;299:853-855.
12. Kuller LH, Simkin-Silverman, L.R., Wing, R.R., Meilahn, E.N., Ives, D.G. Women's healthy lifestyle project; A randomized clinical trial. *Circulation.* 2000(103):32-37.
13. Levine MD, Klem ML, Kalarchian MA, et al. Weight gain prevention among women. *Obesity (Silver Spring).* May 2007;15(5):1267-1277.
14. National Heart Lung and Blood Institute. *The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*: National Institutes of Health; 2000.
15. McTigue KM, Garrett JM, Popkin BM. The natural history of the development of obesity in a cohort of young U.S. adults between 1981 and 1998. *Ann Intern Med.* Jun 18 2002;136(12):857-864.
16. Thomas S, Reading J, Shephard RJ. Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Canadian Journal of Sports Sciences.* 1992;17:338-345.
17. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient. I. Introduction and design. *Br J Cancer.* Dec 1976;34(6):585-612.

18. Meier P. Stratification in the design of a clinical trial. *Control Clin Trials*. May 1981;1(4):355-361.
19. Grizzle JE. A note on stratifying versus complete random assignment in clinical trials. *Control Clin Trials*. 1982;3:365-368.
20. Eiben G, Lissner L. Health Hunters--an intervention to prevent overweight and obesity in young high-risk women. *Int J Obes (Lond)*. Apr 2006;30(4):691-696.
21. Jeffery R, French S. Preventing weight gain in adults: the pound of prevention study. *Am J Public Health*. 1999;89(5):747-751.
22. Diabetes Prevention Program Research Group. The Diabetes Prevention Program: Description of the Lifestyle Intervention. *Diabetes Care*. 2002;25:2165-2171.
- 22a. The Look AHEAD Research Group. The Look AHEAD study: a description of the lifestyle intervention and the evidence supporting it. *Obesity* 2006;14:737-752.
23. Sherwood NE, Jeffery RW, French SA, Hannon PJ, Murray DM. Predictors of weight gain in the pound of prevention study. *Int J Obes*. 2000;24:395-403.
24. Crawford D, Jeffery RW, French SA. Can anyone successfully control their weight? Findings of a three year community-based study of men and women. *Int J Obes Relat Metab Disord*. Sep 2000;24(9):1107-1110.
25. Ball K, Brown W, Crawford D. Who does not gain weight? Prevalence and predictors of weight maintenance in young women. *Int J Obes Relat Metab Disord*. Dec 2002;26(12):1570-1578.
26. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr*. Aug 2006;84(2):274-288.
27. Pereira MA, Kartashov AB, Ebbeling CB, et al. Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet*. 2005;365:36-42.
28. Donnelly JE, Hill JO, Jacobsen DJ, et al. Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch Intern Med*. Jun 9 2003;163(11):1343-1350.
29. Kazdin AE. Self-monitoring and behavior change. In: Mahoney MJ, Thoresen CF, eds. *Self-control: power to the person*. Monterey: Brooks/Cole; 1974.
30. Baker RC, Kirschenbaum DS. Self-monitoring may be necessary for successful weight control. *Behavior Therapy*. 1993 1993;24(3):377-394.
31. D'Zurilla TJ. Problem-solving therapies. In: Dobson KS, ed. *Handbook of cognitive behavioral therapies*. New York: Guilford Press; 1994.
32. Bandura A, Simon KM. The role of proximal intentions in self-regulation of refractory behavior. *Cognitive Therapy and Research*. 1977;1:177-193.
33. Wing RR, Jeffery RW, Burton LR, Thorson C, Sperber Nissinoff K, Baxter JE. Food provision vs. structured meal plans in the behavioral treatment of obesity. *Int J Obes*. 1996;20:56-62.
34. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol*. 1986 1986;124:453-469.
35. Paffenbarger RS, Wing AL, Hyde RT. Physical activity as an index of heart attack risk in college alumni. *Am J Epidemiol*. 1978;108:161-175.
36. Jakicic JM, Marcus M, Gallagher KI, et al. Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. *Med Sci Sports Exerc*. May 2004;36(5):897-904.

37. Stunkard AJ, Messick S. *Eating Inventory Manual*. New York: Psychological Corporation; 1988.
38. Wing RR, Papandonatos G, Fava JL, et al. Maintaining large weight losses: the role of behavioral and psychological factors. *J Consult Clin Psychol*. Dec 2008;76(6):1015-1021.
39. Marcus MD, Wing RR, Lamparski DM. Binge eating and dietary restraint in obese patients. *Addict Beh*. 1985 1985;10:163-168.
40. Williams GC, Grow VM, Freedman ZR, Ryan RM, Deci EL. Motivational predictors of weight loss and weight loss maintenance. *J Pers Soc Psychol*. 1996;70(1):115-126.
41. Levesque CS, Williams GC, Elliot D, Pickering MA, Bodenhamer B, Finley PJ. Validating the theoretical structure of the Treatment Self-Regulation Questionnaire (TSRQ) across three different health behaviors. *Health Educ Res*. Oct 2007;22(5):691-702.
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.
43. Grundy SM. Metabolic syndrome scientific statement by the American Heart Association and the National Heart, Lung, and Blood Institute. *Arterioscler Thromb Vasc Biol*. Nov 2005;25(11):2243-2244.
44. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. Jan 16 2002;287(3):356-359.
45. Turvey CL, Wallace RB, Herzog R. A revised CES-D measure of depressive symptoms and a DSM-based measure of major depressive episodes in the elderly. *Int Psychogeriatr*. Jun 1999;11(2):139-148.
46. Holmes TH, Rahe RH. The social readjustment rating scale. *J Psychosom Res*. 1967 1967;11:213-218.
47. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385-396.
48. Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. *The social psychology of health: Claremont Symposium on applied social psychology*. Newbury Park: Sage; 1988.
49. Wing RR, Phelan S. Behavioral Treatment of Obesity: Strategies to Improve Outcome and Predictors of Success. In: Eckel RH, ed. *Obesity Mechanisms and Clinical Management*. 1 ed. Philadelphia: Lippincott Williams & Wilkins; 2003.
50. Stice E, Orjada K, Tristan J. Trial of a psychoeducational eating disturbance intervention for college women: A replication and extension. *Int J Eating Disord*. Apr 2006;39(3):233-239.
51. Stice E, Presnell K, Groesz L, Shaw H. Effects of a weight maintenance diet on bulimic symptoms in adolescent girls: an experimental test of the dietary restraint theory. *Health Psychol*. Jul 2005;24(4):402-412.
52. Tooze JA, Grunwald GK, Jones RH. Analysis of repeated measures data with clumping at zero. *Stat Methods Med Res*. Aug 2002;11(4):341-355.
53. Sallis JF, Haskell WL, Wood PD, et al. Physical activity assessment methodology in the Five-City Project. *Am J Epidemiol*. Jan 1985;121(1):91-106.

54. Leenders NY, Sherman WM, Nagaraja HN, Kien CL. Evaluation of methods to assess physical activity in free-living conditions. *Med Sci Sports Exerc.* 2001;33(7):1233-1240.
55. Littell RC, Milliken GA, Stroup WW, Wolfinger RD. SAS System for Mixed Models. Cary, NC: SAS Institute Inc., 1996.
56. Baron RM, Kenny DA. The moderator-mediator distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Personal Soc Psychol* 1986;51:1173-82.
57. MacKinnon DP. Contrasts in multiple mediator models. In *Multivariate Applications in Substance Use Research: New Methods for New Questions* ed. JS Rose, L Chassin, CC Pressib, SJ Sherman, p141-60. Mahwah, NJ: Erlbaum, 2000.
58. Huang B, Sivaganesan S, Succop P, Goodman E. Statistical assessment of mediational effects for logistic mediational models. *Statist Med* 2004;23;2713-2728.