

CALERIE II Study Information

At today's visit, you signed and reviewed the screening consent form. This only covers what will occur during the screening phase of the study. We have developed this handout as a way to help you better understand what will happen beyond the screening phase. Please use this information to help you make a decision about participation in our CALERIE program.

Please read over the information carefully and also visit our website at <http://calerie.pbrc.edu>

Additional Study Information

The overall purpose of this study is to gain knowledge about the effects of two years of food restriction in reducing the risk of disease associated with aging and in slowing of the aging process.

It has been reported for many years that sustained caloric restriction without nutritional deficiencies increases the length of life and prevents development and/or progression of some age-related chronic diseases such as cancer, diabetes and cardiovascular disease in a variety of animals. Whether this occurs in humans, is not known. This study is designed to determine the effects of sustained caloric restriction on physiology, metabolism, body composition, risk factors for age-related diseases, progression of age-related changes, and potential adverse effects in non-obese humans. It is already known that weight loss improves insulin sensitivity and the lipid profile.

Once you have successfully completed the screening phase of the study, you will be asked to return for baseline testing. Following successful completion of the baseline testing, you will be enrolled in the two-year CALERIE study.

For enrollment into the study, you will be randomly assigned to one of two groups for the next 24 months. By "random", we mean that neither you nor any of the staff (including the doctor) can select the group you will be in. Using a procedure, like flipping a coin, a computer program assigns you to one of the groups. You will keep this group assignment for the remainder of the study. Participants will be assigned in a 2:1 ratio (meaning 2 people will be assigned to group 2 for every 1 person assigned to group 1).

1. Group One: The "regular diet" group will be instructed to continue to follow their regular diet as always and no modifications to their diet will be made. You have one in three chances to be assigned to this group.
2. Group Two: Group two will be the "calorie-restricted" group (CR). This group will be placed on a calorie-restricted diet, with 25% fewer calories than their measured baseline energy requirements. You have two in three chances to be assigned to this group.

If you are in the CR group, you will receive all your food for the first month after randomization. Over the next 2 years, you will be expected to lose approximately 15% of your body weight (example: 24 pounds for a 160 pound person). You will also receive weekly counseling sessions on a personal basis and one session with the other participants enrolled in the same group to help you with any problems that make it difficult to complete the program. You will be asked to fill out a food record daily and bring it to all of the counseling sessions. The following table explains the minimum frequency for counseling sessions:

Month	Individual Session	Group Session
Month 1	At least once per week	At least 1 group sessions
Month 2-6	At least twice per month	At least 2 group sessions per month
Month 7-12	At least twice per month	At least 1 group session per month
Month 13-24	At least once per month	At least 1 group session per month

If you are in the "regular diet group", you will be responsible for making your own food selections and preparing your own meals. You will not be required to return for frequent dietary counseling.

Whatever group you are assigned to, you will be requested to return for scheduled clinic and inpatient visits. In between the clinic visits, if you are in the calorie restricted group, you will be asked to weigh yourself at home weekly (daily during the doubly labeled water periods) on the scales provided to you by study personnel and keep an on-going record of your home weights. If you are in the "regular diet group", you will be requested to weigh yourself daily during each doubly labeled water period for 14 days. These weight records should be brought in with you to your scheduled clinic visits.

Procedures/Tests That Will Occur Over the Course of the Study

- **Blood pressure, heart rate, temperature, waist measurements and respirations.**
- **Body composition and bone mineral density by DEXA:** This test involves changing into a hospital gown, removing any metal objects and lying on a table called a DEXA scanner. This scanner uses low-dose x-rays to determine the amount of fat, bone and muscle in your body. Results of this test are used in the calculations of your adherence to the diet you are assigned.
- **Doubly-Labeled Water (DLW):** This test measures your total energy expenditure over a 14 day period through the collection of urine samples. At each DLW dose, you will be requested to provide a urine sample, before drinking a glass of water that is enriched with two atoms which are called stable isotopes (non-radioactive). The rest of the day, you will be asked to provide periodic urine samples. Measures of the 2 atoms in your urine will tell us how many calories you are burning. This value will be used to estimate your daily caloric intake over the next 2 years.
- **Resting Metabolic Rate:** Your resting metabolic rate is the number of calories you burn while resting in bed. This test involves lying quietly while breathing normally with a clear canopy (a large plastic hood) placed around your head for about 45 minutes to 1 hour. The hood is ventilated with fresh room air. This will permit the measurement of how much oxygen you breathe in and how much carbon dioxide (CO₂) you breathe out.
- **VO₂ Max:** Your aerobic fitness level will be assessed while you run on a treadmill. Following a 5 minute warm-up, you will run at a comfortable pace and grade that will progressively get harder each minute until you are winded and unable to continue. During the test, the volume of oxygen intake and carbon dioxide (CO₂) production will be measured continuously using a metabolic cart, a non-invasive equipment that is also used to measure your metabolic rate. The test requires a mouthpiece which you will breathe through and a nose clip during the exercise test. Your heart rate will also be monitored continuously using a heart rate monitor.
- **Oral Glucose Tolerance Test:** The oral glucose test will be done to measure your body's response to glucose (sugar). Before you eat breakfast you will drink a glucose beverage and have blood drawn every 30 minutes for 2 hours. You will be asked to consume a high carbohydrate diet (at least 150 grams of carbohydrates) for approximately three days prior to this testing.
- **Muscle Strength Testing:** To test your leg strength, you will be asked to press against a bar as hard as possible and lifting as much weight as possible. Your grip strength will also be measured by squeezing a hand grip tool.
- **Psychological Testing:** You will be given several forms to complete at your clinic visit. Some of the questionnaires ask explicit questions related to mood, eating behavior, weight control strategies, sexual functioning and other similar topics. You may either honestly answer these questions or you may choose to not answer the questions. You will also complete computerized tasks to determine how you feel about your body.
- **Cognitive Testing:** You will be given several forms to complete and short tasks to do. You will be asked to provide word definitions, repeat aloud numbers and object/animal names that are read to you, answer background information questions (i.e. age, occupation, highest education, level achieved, etc.) and other questions pertaining to your cognitive and emotional state. Additional cognitive tasks will be performed to determine how you process information.
- **Core Temperature:** During overnight stays, your internal body (core) temperature will be monitored by swallowing a small silicone coated radio capsule. This capsule will constantly send a radio signal to a recorder worn on your belt to record your core temperature for 24 hours. The capsule normally remains in the body for 24-72 hours and will be passed as you move your bowels.
- **Immune Function Testing:** Immune status, an indicator of the body's ability to fight infection, will be assessed from measurements of delayed type hypersensitivity response (DTH), examination of the blood cells and response to vaccines. The DTH test is similar to an allergy or tuberculosis skin test. In addition, three different vaccines (hepatitis A, pneumococcus, and tetanus/diphtheria) will be administered at Month 17. A booster shot of the Hepatitis A vaccine will be administered at 23 months. Blood will be collected at baseline, months 17, 18, 23 and 24 for measurement of antibodies. Your body's antibody levels, in response to the three vaccines, are another way to assess your immune status.

Participant Schedule

- **Screening**
 - Screening Visit 1 – approx 2 hours
 - Screening Visit 2 – approx 3-6 hours
 - Screening Visit 3 – approx 1 hour
- **Baseline (5 consecutive weeks)**
 - Baseline Visit 1 & 2 – approx 7 hours
 - Baseline Visit 3 – approx 2 hours
 - Baseline Visit 4 – approx 7 hours
 - Baseline Visit 5 – approx 2 hours
 - Baseline Visit 6 – Evening Admit to Inpatient Unit
 - Baseline Visit 7 – 24 hr Inpatient Stay
 - Baseline Visit 8 – Inpatient testing – D/C in afternoon
 - Additional night/day stay for Ancillary study – Chamber
- **If you are randomized to the Caloric Restricted Group**
 - You will come to the Pennington Center for breakfast and dinner (with lunch and weekend meals packaged to go) for 27 days.
 - Please refer to page 1 for detailed information on the frequency of intervention sessions.
- **Month 1**
 - Visit 1 – approx 1 hour
- **Month 3**
 - Visit 1 – approx 1 ½ hours
- **Month 6**
 - **CR Group**
 - Visit 1 – approx 6 ½ hours
 - Visit 2 – 1 hour
 - Visit 3 – Afternoon admit to Inpatient Unit
 - Visit 4 – Inpatient Test day afternoon D/C
 - **Control Group**
 - Visit 1 – Afternoon admit to Inpatient Unit
 - Visit 2 – Inpatient Test day afternoon D/C
- **Month 9**
 - Visit 1 – approx 1 hour
- **Month 12 (2 consecutive weeks)**
 - Visit 1 – approx 6 ½ hours
 - Visit 2 – approx 2 hours
 - Visit 3 – Evening Admit to Inpatient Unit
 - Visit 4 – 24 hour Inpatient Stay/Test Day
 - Visit 5 – Inpatient Test day afternoon D/C
 - Additional night/day stay for Ancillary study - Chamber
- **Month 17**
 - Off-schedule Evaluation – Vaccination Day
- **Month 18**
 - **CR Group**
 - Visit 1 – approx 6 ½ hour
 - Visit 2 – approx 1 hour
 - Visit 3 – Afternoon Admit to Inpatient Unit
 - Visit 4 – Inpatient Test day, D/C afternoon
 - **Control Group**
 - Visit 1 – approx 1 hour
- **Month 23**
 - Off-schedule Evaluation – Vaccination Day
- **Month 24 (2 consecutive weeks)**
 - Visit 1 – approx 6 ½ hours
 - Visit 2 – approx 2 hours
 - Visit 3 – Evening Admit to Inpatient Unit
 - Visit 4 – 24 hour Inpatient Stay/Test Day
 - Visit 5 – Inpatient Test day afternoon D/C
 - Additional night/day stay for Ancillary study - Chamber