

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title of Study: Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) Phase II – Screening Phase

What you should know about a research study

- We give you this consent form so that you may read about the purpose, risks and benefits of this research study.
- The main goal of research studies is to gain knowledge that may help future patients.
- You have the right to refuse to take part, or agree to take part now and change your mind later on.
- Please review this consent form carefully and ask any questions before you make a decision.
- Your participation is voluntary.
- By signing this consent form, you agree to participate in the study as it is described.

1- Who is doing the study?

Investigator Information:

Principal Investigator: Eric Ravussin, Ph.D.
225-763-3186

Medical Investigator: Alok Gupta, M.D.
Day Phone: 225-763-2656
24-hr. Emergency Phone Nos.:
225-763-2656 (Weekdays 7:00a.m.-4:30 p.m.)
225-765-4644 (After 4:30 p.m. and Weekends)

Co-Investigators: Donald Williamson, Ph.D.
Steven Smith, M.D.
Corby Martin, Ph.D.

Dr. Eric Ravussin directs this study, which is under the medical supervision of Dr. Alok Gupta. We expect about 250 people from 3 sites (Pennington, Tufts University in Boston and Washington University in St. Louis) to be enrolled in this study. Pennington expects to enroll approximately 84 people at this site. The study will take place over a period of 6 years. Your expected time in this study will be approximately 2 ½ years. This study is part of ongoing research in the prevention and treatment of age-related diseases at the Pennington Center and is being funded by the National Institute on Aging.

2- Where is the study being conducted?

This study takes place at the Pennington Biomedical Research Center's inpatient and outpatient clinics and the Pennington Metabolic Kitchen.

3- What is the purpose of this study?

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.

The purpose of the screening visits is to assess your eligibility for participation in the CALERIE Study.

4- Who is eligible to participate in the study? Who is ineligible?

You may qualify for this study if you meet the following criteria:

- Your BMI (your height to weight ratio) is $\geq 22 \text{ kg/m}^2$ and $< 28 \text{ kg/m}^2$.
- You are a male age 21 to 50 or a female age 21 to 47.
- You are willing to postpone pregnancy for 2.5 years.

You will not qualify for the study if any of the following applies to you:

- You have a history of cardiovascular disease or an elevated blood pressure (greater than 140/90 mm Hg).
- You have an abnormal ECG.
- You have low bone mineral density as shown in your DEXA scan during the baseline testing.
- You have a history of diabetes, gall stones or any other significant metabolic, hematologic, pulmonary, cardiovascular, gastrointestinal, neurologic, immune, hepatic, renal, urologic disorders, or cancer.
- You have a history of stomach or intestinal surgery (except appendectomy) or major abdominal, thoracic or non-peripheral vascular surgery within one year prior to enrollment into the CALERIE study.
- You have any disease or condition that seriously affects body weight and/or body composition.
- Your potassium level is above the upper limit of normal at the screening visit and is confirmed by a repeated test within 2 weeks of the original.
- Your hemoglobin, hematocrit, red blood cell count, or iron level is below the lower limit of normal at the screening visit and is confirmed by a repeat test within two weeks of the original test.

- You show evidence of active liver disease or liver enzyme levels above 1.5 times the upper limit of normal.
- Your LDL Cholesterol is \geq 190 mg/dl at the screening visit.
- You have a history of any eating disorder as determined by questionnaires you answer and interviews at the screening visits.
- You have a history of pharmacologic treatment for a psychiatric disorder within one year prior to the randomization date or a history of more than one episode of a pharmacologic treatment for a psychiatric disorder within your lifetime.
- You have a history of drug or alcohol abuse (up to 14 drinks a week are allowed) within the past two years.
- You scored \geq 20 on the Beck Depression Inventory questionnaire at screening.
- You have any significant behavioral and/or clinical barrier to effective participation in the study as identified by the Barriers to Effective Intervention Interview.
- You have a history of short-term (less than a month) treatment with steroids within six months prior to your randomization into CALERIE Phase II.
- You have a history of treatment with steroids for more than a month within five years prior to your randomization into CALERIE Phase II.
- You require regular use of medications other than contraceptives.
- You participated in CALERIE Phase I studies.
- You smoke or quit smoking less than 12 months prior to screening.
- You have donated blood within 30 days prior to randomization into the study.
- You are participating in another intervention program.
- You are pregnant, breast feeding or planning to become pregnant before the end of the study.
- You engage in a regular physical fitness program involving some kind of heavy physical activity (e.g. jogging, running or riding fast on a bicycle for 30 minutes or more) five or more times per week over the past year.
- You are unwilling to be assigned at random to the CR or control intervention.
- You are unwilling or unable to adhere to the rigors of the CR intervention over the entire two-year period.
- You are unable or unwilling to discontinue dietary supplements or adhere to the alcohol consumption restrictions during the study.
- You are unwilling or unable to adhere to the rigors of the data collection and clinical evaluation schedule over the two-year follow-up period.
- You are female and unwilling to use an acceptable form of contraception (acceptable forms include: tubal ligation, partial or complete hysterectomy, barrier method, oral contraceptive, intrauterine device, implanted progesterone, contraceptive vaginal ring, spousal vasectomy, abstinence or natural family planning when other contraceptive methods are prohibited due to religious reasons) and continue to use such methods while enrolled in the study.

5- What will happen to you if you take part in the study?

The screening process will consist of three separate visits that enable us to assess your eligibility for participation in the CALERIE Study. The entire screening process should take approximately 6 hours total plus transportation time and may incorporate up to a 3 month time period to complete all visits.

Screening Visit 1 – Approximately 2 hours

The first visit in the screening process will involve measuring your height and weight. You will be asked to remove your shoes and outer-garments and to empty your pockets. If your weight is within a certain range relative to your height (called body mass index or abbreviated to BMI), you will be eligible to continue with the screening process. If your weight is not within this range, you will not be eligible to continue with the screening process and participate in the study.

If you meet the weight eligibility requirements, you will be asked to complete several questionnaires related to your lifestyle, weight history, eating habits, personality, mood and physical activity. A demographic questionnaire will be given that will ask about your date of birth, your primary physician and other personal information. A calendar will be given to you so you can fill out your work schedule and personal obligations. You will have a brief interview with the study dietician to determine any food allergies, gastrointestinal conditions, alcohol consumption and current nutritional supplements. The study will also be described to you and what your participation in the study would involve.

Screening Visit 2 – Approximately 2 hours

On your second screening visit, you will be asked to not eat or drink anything for 12 hours prior to your visit. A blood sample (approximately 2 tbsps) will be drawn for hematology, blood chemistry, and a pregnancy test (if you are female). An electrocardiogram (ECG) will be done to evaluate your heart. You will be asked to provide a urine sample. At this visit you will undergo a fasting weight measurement in the clinic, a brief physical exam by a study physician and your blood pressure, heart rate, temperature, and respiration will be measured. A complete medical history will be performed and will include a review of all major organ systems, contraceptive and menstrual history for women, questions about your current health, health history and any medications you may be taking. You will be provided breakfast at the completion of your blood work and the physical exam.

During the second screening visit you will meet with a behavioral specialist and undergo a behavioral and psychological interview. During this interview a computer based body assessment procedure will be performed during which you will be shown a computer images of your body at a much leaner and/or fatter state.

You will again meet briefly with the study dietician who will instruct you on maintaining a 14-day food record at home and ask you to bring this completed record back on the third screening visit. Verbal and written instructions will be given by the dietician for you to follow once you leave the clinic.

Screening Visit 3 – Approximately 2 hours

The third screening visit will consist of a review of your 14 day food record with the study dietician. You must successfully complete this diary in order to be eligible to continue in the CALERIE study. Also, a final overview of all questionnaires, interviews, blood work, and physical exam findings will be discussed from earlier screening visits. After successfully completing the above assessments, your data will be reviewed and you will be contacted by phone as to whether you meet all the requirements to participate in this study.

6- What are the possible risks and discomforts?

There are certain risks and discomforts that may be associated with the screening process. They include the following:

- Likely:
 - Interview assessments – could cause fatigue and possible anxiety. Fatigue will be kept to a minimum by keeping the interview sessions brief and allowing short breaks. You may also refuse to answer any question which causes you to become nervous or upset (or become anxious).
- Less Likely:
 - Questionnaires – the questions contained in some of the questionnaires may make you feel uncomfortable. Your responses to the research questions will be coded to protect your confidentiality. Some questionnaires ask explicit questions related to mood, eating behaviors, weight control strategies, sexual functioning and other similar topics. You may either honestly answer these or you may choose not to answer them.
 - Blood Drawing – you may experience discomfort, bruising and/or bleeding at the needle insertion site. Occasionally some people experience dizziness or feel faint. There is an extremely small chance of an infection developing at the needle insertion site.

Participation in the screening process of this study may cause all or some of the side effects listed above. In addition, there is always the risk of developing previously unknown side effects.

The investigator is willing to discuss any questions you might have about the severity, frequency and the duration of these risks and discomforts.

7- What are the possible benefits?

We cannot promise any benefits from your being in the screening phase of the study. However, possible benefits include receiving information about your health from blood work results and ECG findings. Also, successful completion of the screening portion of this study will enable you to progress to the next phase, which is participation in the study.

8- If you do not want to take part in the study, are there other choices?

You have the choice at any time not to participate in this research study. If you choose not to participate, any health benefits to which you are entitled will not be affected in any way.

9- If you have any questions or problems, whom can you call?

If you have any questions about your rights as a research volunteer, you should call the Institutional Review Board Office at 225/763-2693 or Dr. Claude Bouchard, Executive Director of PBRC at 225/763-2513. If you have any questions about the research study, contact Dr. Eric Ravussin (Principal Investigator) at 225/763-3186. If you think you have a research-related injury or medical illness, you should call Dr. Alok Gupta at 225/763-2656 during regular working

hours. After working hours and on weekends you should call the answering service at 225/765-4644. The on-call physician will respond to your call.

10- What information will be kept private?

Every effort will be made to maintain the confidentiality of your study records. However, someone from the National Institutes of Health, National Institute on Aging, the Pennington Biomedical Research Center, and the Coordinating Center at Duke University may inspect and/or copy the medical records related to the study. Results of the study may be published; however, we will keep your name and other identifying information private. Other than as set forth above, your identity will remain confidential unless disclosure is required by law.

Since the study is sponsored, a representative of the funding agency, National Institute on Aging (NIA) may inspect these research records. Duke Clinical Research Institute (DCRI) acting as the coordinating center for this study may also inspect your research records. Your screening blood work will be sent to a central laboratory (Labcorp) for processing but your samples will only be identified by a subject ID number and will not include any personal identifiers.

All study related data will be transferred into a centralized database at DCRI. Only authorized personnel at DCRI will have access to the files containing these data. Your information will be accessed through user logon IDs, passwords and appropriate access privileges to promote security. All study participants will be identified by their study ID number and no personal identifying information, such as name, address, telephone numbers, etc., will be entered into the coordinating center's database. Any participant's specific data that is reported to study leadership will be identified only by a study ID number.

Finally, participants will not be identified in any study reports or publications, nor will the data be presented in such a way that the individual participant could be identified. All participants' identifiers will be removed from any files created for further scientific study.

If you decide to discontinue your participation in the study before your two-year commitment is over and you do not want your information used in study analyses or shared with other centers as stated above, then you must provide this in writing to Dr. Eric Ravussin at Pennington.

The research team may use and share your information until 5 years after closure of the study. All that time afterwards, the research information in your records will be destroyed or information identifying you will be removed, making it impossible to link you to the study.

11- Can your taking part in the study end early?

Drs. Eric Ravussin and Alok Gupta or the study sponsor can withdraw you from the study for any reason or for no reason. You may withdraw from the study at any time without penalty. Possible reasons for withdrawal include inability or unwillingness to continue participation and adherence to the required screening procedures. The sponsor of the study may end the study early.

12- What if information becomes available that might affect your decision to stay in the study?

During the course of this study there may be new findings from this or other research which may affect your willingness to continue participation. Information concerning any such new findings will be provided to you.

13- What charges will you have to pay?

None

14- What payment will you receive?

None

15- Will you be compensated for a study-related injury or medical illness?

No form of compensation for medical treatment or for other damages (i.e., lost wages, time lost from work, etc.) is available from the Pennington Biomedical Research Center. In the event of injury or medical illness resulting from the research procedures in which you participate, you will be referred to a treatment facility. Medical treatment may be provided at your expense or at the expense of your health care insurer (e.g., Medicare, Medicaid, Blue Cross-Blue Shield, Dental Insurer, etc.) which may or may not provide coverage. The Pennington Biomedical Research Center is a research facility and provides medical treatment only as part of research protocols. Should you require ongoing medical treatments, they must be provided by community physicians and hospitals.

This research is not intended for the purpose of diagnosing or treating any medical problems, not specifically stated in the purpose of the research. Participation in a research study does not take the place of routine physical examinations or visits to your personal physician.

16- HIPAA

Records that you give us permission to keep, and identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in records disclosed outside of Pennington Biomedical Research Center (PBRC). For records disclosed outside of PBRC, you will be assigned a unique code number.

Protected Health Information (PHI) is any health information through which you can be identified. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). A decision to participate in this research means you agree to allow the research team to use and share your PHI for the study explained above. The research team will look at your hospital/medical records (in-patient), laboratory, pathology and/or radiology sample results, questionnaires/interviews, and other pertinent medical information and record such information needed for the study in the research file. Your research file will contain information such as your initials, subject ID # and date of birth. PHI may be shared with individuals involved in the research study.

17- Signatures

The study has been discussed with me and all my questions have been answered. I understand that additional questions regarding the study should be directed to the study investigators. I agree with the terms above and acknowledge that I have been given a signed copy of the consent form.

With my signature, I also acknowledge that I have been given either today or in the past a copy of the Notice of Privacy Practices for Protected Health Information.

Signature of Volunteer

Date

Date of Birth of Volunteer

Signature of Person Administering Informed Consent

Date

Eric Ravussin, Ph. D.
Principal Investigator

Alok Gupta, M.D.
Medical Investigator