

___ Minimal Risk

___ At Risk

RESEARCH CONSENT FORM

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Name of Participant:

Date:

Title of Study: CCRC: The Metabolic Effects of Consuming Sugar-Sweetened Beverages for Two Weeks

Principal Investigator: Peter J. Havel

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a medical research study. As an experimental subject, you have the following rights:

- 1) To be told what the study is trying to determine.
- 2) To be told what will happen to you and whether any of the procedures, drugs, or devices is different from what would be used in standard practice.
- 3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to you for research purposes.
- 4) To be told if you can expect any benefit from participating and, if so, what the benefit might be.
- 5) To be told the other choices you have and how they may be better or worse than being in the study.
- 6) To be allowed to ask any questions concerning the study, both before agreeing to be involved and during the course of the study.
- 7) To be told what sort of medical treatment is available if any complications arise.
- 8) To refuse to participate or to change your mind about participating after the study is started. This decision will not affect your right to receive the care you would receive if you were not in the study.
- 9) To receive a copy of the signed and dated consent form.
- 10) To be free of pressure when considering whether you wish to agree to be in the study.

If you have other questions, please ask the researcher or research assistant. You may also ask the UC Davis Institutional Review Board (IRB) or the VA Northern California Health Care System Human Research Protection Program (HRPP). The IRB and HRPP protect volunteers in research projects. You may call the UCD IRB at (916) 703-9151 or the VA HRPP at (916) 366-5359 from 8:00 a.m. to 4:30 p.m. Monday through Friday. You may also call VA Regional Counsel at (415) 750-2288. You may write to the UCD IRB at: University of California, Davis, IRB Administration, CTSC Building, Suite 1400, Rm. 1429, 2921 Stockton Blvd., Sacramento, CA 95817 or the VA HRPP at: VANCHCS HRPP (151), 10535 Hospital Way, Bldg. 807, Mather, CA 95655.

Signature of Participant

Date

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SUBJECT'S IDENTIFICATION (I.D. give name - last, first, middle; address and phone number)

Name of Participant:

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Title of Study: CCRC: The Metabolic Effects of Consuming Sugar-Sweetened Beverages for Two Weeks

Principal Investigator: Peter J. Havel

PURPOSE OF THE STUDY

This is a research study. Research studies only include subjects who choose to take part. You do not have to be in this research study. You should read the information that follows. Please ask questions about anything you do not understand before deciding if you want to be in this research study. Please take your time to make your decision. Discuss it with your friends and family.

We are asking that you take part in a research study of sugar. The purpose of this study is to learn more about the effects of consumption of sugar-sweetened beverages. We will study if consumption of sugar-sweetened beverages has effects on your blood triglycerides and cholesterol and cholesterol concentrations, and your body's sensitivity to the hormone insulin. We will also study how sugar-sweetened beverages affect your body's capacity to burn calories.

We are asking you to take part in this study because you are a nonsmoker who does not have diabetes mellitus or liver, kidney or thyroid disorders, or take hypolipidemic, anti-diabetic anti-hypertensive or anti-depression medication. You must be between the ages of 18-40 years. In order to participate in this study, it will be necessary to give your written consent.

RESEARCHER'S DISCLOSURE

Non-profit: Peter Havel, DVM, Ph.D. from the UC Davis Department of Biomolecular Sciences, Veterinary Medicine is conducting the study. The National Institute of Health, a non-profit agency that promotes scientific research, is funding this clinical study. This means that the National Institute of Health is giving money to the University so that Dr. Havel can conduct the study.

STUDY PROCEDURES

About 200 people will take part in this study. We will study men and women who are normal weight, and men and women who are overweight. We will study the effects of consuming different amounts of sugar. Therefore participants in this study will consume sweetened beverages that contain either 1) no sugar, 2) a low amount of sugar, 3) a medium amount of sugar, 4) a high amount of sugar. Participants will not know which sugar group they have been assigned to because all beverages will be made equally sweet using a non-caloric sweetener such as Splenda. This study will be called "DRS", which is short for "Dose Response Sugar Study."

Study Duration

Participation in the study will take a total of about 210 hours over a period of 20 to 27 days.

If you volunteer to take part in this study, we will ask you to do the following things:

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Before you begin the main part of the study.

You will need to have the following "screening" exams, tests or procedures to find out if you can be in the main part of the study. These tests will occur during the screening visit at the University of California, Davis Clinical and Translational Science Center Research Center (CCRC). The CCRC is part of the Sacramento Veterans' Affairs (SVA) Hospital (located off of Mather Field exit on US 50) and it was built for the purpose of allowing the Physicians and Professors at SVA and University California Davis to conduct research studies such as this one. For the tests to be valid, it will be necessary for you to follow these dietary guidelines:

Do not consume alcoholic beverages the day before the screening visit.

Do not eat or drink anything except water before the study visit starting at 8PM the night before.

- **Medical history questionnaire:** You will be asked to fill out a questionnaire about your medical history.
- **Physical Activity questionnaire:** You will be asked to fill out a questionnaire about your general physical activity.
- **Blood drawing (venipuncture):** You will be asked to give a blood sample for laboratory tests. Approximately 2 teaspoons of blood will be drawn by inserting a needle into a vein in your arm for these tests. At this time the nurse will assess the suitability of your veins for the multiple blood draws that are required for some of the experimental study procedures.
- **Pregnancy testing:** Because some of the experimental procedures may affect a fetus, and because pregnancy can affect the study results, pregnant women may not participate in this study. If you are a female and have had your first menstrual period, a urine test will be done at the initial visit and subsequently on Study Day 1 to make sure you are not pregnant.
- **CCRC visit:** The above tests will occur at the University of California, Davis Clinical and Translational Science Center Research Center (CCRC). The CCRC is part of the Sacramento Veterans' Affairs (SVA) Hospital (located off of Mather Field exit on US 50) and it was built for the purpose of allowing the Physicians and Professors at SVA and University California Davis to conduct research studies such as this one. Participation in this study requires that you spend a total of 140 hours at the CCRC, consisting of an 80-hour period at the beginning of the study, a 2.5-hour period in the middle of the study, and an 80-hour period at the end of the study. You will be shown a calendar of study dates, and asked to indicate the dates that you will be available to participate. You will be given a short tour of the CCRC, to allow you to determine whether you are willing to commit to spending the required amount of time at the CCRC. Most likely, you will share a bedroom with another study participant during this time. You will also be given a list of the foods that you will be required to eat while you are staying at the CCRC, to allow you to determine whether you are willing to commit to eat them.

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If the screening exams, tests or procedures show that you can continue to be in the study, and you are selected to participate, you will be scheduled into the study. You will be asked to not drink sugar beverages for the 5 weeks before your study start date with the exception of 8 ounces of naturally sweetened fruit juice/day. If you normally drink 2 or more servings of sugar-sweetened beverages/day, you will be asked to report to the CCRC 1 week before the study start day for a 2nd fasting blood draw. If your blood values indicate decreased sugar consumption compared to the blood values from the earlier screening, you will be accepted into study.

- A subset of the participants in this study will be selected to participate in an additional procedure for measuring total daily caloric expenditure. Participation in this aspect of the study requires spending two 23-hour periods in the Whole-Room Calorimeter (located on the UC Davis campus). While in this room, your body's oxygen consumption and carbon dioxide production will be measured. You will be shown pictures of the Whole-Room Calorimeter in order to allow you to determine whether you are willing to spend 23 hours at the beginning of the study and 23 hours at the end of the study in this room. Unwillingness to participate in this procedure will not affect your eligibility to participate in the study. If you are willing to participate in this procedure, we will make arrangements for you to see the Whole-Room Calorimeter and have a brief orientation about the test day schedule prior to making a final decision to participate in this aspect of the study.

During the main part of the study.

If the screening exams, tests or procedures show that you can continue to be in the study, and you choose and are selected to take part, then you will have the following tests and procedures done.

- **Inpatient Diet - Standardized:** During Study Days 3, 4, 19, 20 you will be served a standardized diet based on your calculated energy requirement. You will need to eat only and all of the food provided on these days.
- **Inpatient Diet – Non-Standardized Buffet with Appetite Assessment:** During Study Days 2 & 18 your meals will be served buffet-style and you will help yourself to as much or as little as you want to eat. During these days you will be asked to record your feelings of hunger, fullness, and desire to eat and drink, using a pen and a hand-held computer with a visual scale, immediately before and after each meal and one time per hour at other times.
- **Sugar-sweetened beverages:** Starting on the 5th day of the study through to the end of study, you will drink a sweetened beverage with each meal. These beverages will be provided to you as 3 servings/day, approximately 12-16 fluid ounces at each meal. In order for this study to produce scientifically useful information, it is necessary that you consume all 3 of the beverages provided each day. The sweetened beverages will contain a biomarker, and urine will be collected and analyzed for the biomarker in order to confirm that all beverage is being consumed.

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Metabolic Rate Monitoring in the Whole-Room Calorimeter: If you are willing, and if you are selected to participate in the Whole Room Calorimeter procedures, on the first day of the study and on the final day of the study, your oxygen consumption and carbon dioxide production will be measured continuously for 23 hours while you remain inside a small room specially constructed for this purpose. These measurements will allow us to determine your metabolic rate throughout the day and to see how it is affected by consumption of meals and the sugar-sweetened beverages. This room is located in the Western Human Nutrition Research Center Building at 430 W. Health Sciences Drive on the west side of the UC Davis campus. The calorimeter room is approximately 9 ft by 9 ft – about the size of a small bedroom. It contains a bed, desk, chair, TV/DVD, wireless internet, sink, toilet, and privacy screen. The room also has two large windows with mini-blinds for privacy; one window looks to the outdoors and the other looks to the indoor area surrounding the room where the research staff work. The 23-h monitoring period will begin around 8 AM and end 7 AM the next day. Standardized meals will be served at 9 AM, 1 PM, and 6 PM. Only one study participant can be monitored at a time in the whole-room calorimeter. Therefore, we will only be studying a subset of participants, and for these participants, the duration of the study and the number of days that you will continue to drink the sugar-sweetened beverages following Study Day 22 are dependent on when you are scheduled for your second day of metabolic rate monitoring.

As part of your stay in the calorimeter, you will be asked to do some procedures that are needed for metabolic rate monitoring including:

- 1) Collect all urine that you pass for the time you are in the chamber. Special containers will be provided to you.
- 2) . Provide information about your mood and appetite. A Palm pilot will alert you on an hourly schedule and present questions so you can record how you are feeling, how hungry you are, and evaluate the quality of your meals.
- 3) Wear an activity monitor. The monitor records your movements, is about the size of a quarter, and attaches to an elastic strap worn around the waist.
- 4) Provide 10 saliva samples at specific times during your stay. Cotton swabs will be provided for saliva sampling.
- 5) You will perform three 10-minute intervals of moderate activity using a stair-stepper mid-morning, early afternoon, and approximately one hour before dinner.
- 6) One additional procedure, a treadmill test to estimate your maximal aerobic capacity, will be done once following your second test in the whole room calorimeter. After you leave the calorimeter at 7AM, we will provide a small breakfast in the WHNRC dining room, and 30-40 minutes after breakfast we will explain the test in detail and then conduct the test in the WHNRC physiology lab. The test consists of walking on the treadmill at a pace of about 3 miles per hour; the grade of the treadmill will be flat to begin with and will increase 2 ½ % every 3 minutes until you reach a level of exertion that is 'somewhat hard' or 'hard' and your heart rate is 85% of your age-predicted maximum heart rate. This test is called a 'submaximal treadmill test' and allows us to predict your maximal aerobic capacity. During the time you are walking you will be breathing into a mouthpiece that allows

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us to trap the air that you breathe out. We will also monitor your heart rate with a heart rate monitor and take your blood pressure every 3 minutes. The length of this test will range about 12 to 18 minutes, depending on your level of fitness.

- Pre- and Postheparin Blood Draws:** On Study Day 2 and 18, a fasting blood sample (1/2 tsp) will be collected at 8AM from an arm vein by venipuncture. Heparin, a blood thinner, will be injected into the vein of your other arm. Another blood sample (1/2 tsp) will be collected about 15 minutes later. The same procedure will be repeated on Study Days 3 and 19, excepting that it will be performed at 10:00PM. These pre- and postheparin blood samples will be measured for lipase, an enzyme that is involved in fat metabolism.
- DEXA:** The composition of your body (lean, fat, mineral) will be measured using dual energy X-ray absorptiometry (DEXA). You will lie on a padded table that is above an x-ray tube that will scan your body, measuring the amount of x-rays that pass through for 5 to 10 minutes. The level of radiation for each DEXA procedure is less than that of a cross-country airplane flight. This test will be performed on Study Day 2.
- Fat Biopsies:** We will obtain a very small (1/10 of an ounce) piece of fat from under the skin in your gluteal region (buttocks). A local anesthetic will first be injected to desensitize the area, and then the tissue will be withdrawn through a needle into a syringe. It may be necessary for the physician to insert the needle 2 times to withdraw the needed amount of fat. Fat biopsies will be collected four times during the study; on Study Day 3 at 8AM and at 8PM, and on Study Day 19 at 8AM and at 8PM.
- CT scan:** You may have a computed tomography (CT) scan of your stomach, done on Study Day 3, in order to measure your distribution of subcutaneous fat (fat outside the body cavity) and visceral fat (fat within). A CT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. The instrument to conduct this measurement is located at University of California Davis Medical Center, and a member of the study team will drive you there. This procedure will only be performed on a small subset of subject (about 20-30), and results will be compared with the results obtained by the MRI scan (described below).
- MRI:** On Study Days 3 and 19, you will have a Magnetic Resonance Imaging (MRI) exam to measure the amount of fat in your liver. You will also have a Magnetic Resonance Imaging (MRI) exam of your abdomen to determine extra and intra-abdominal fat volume. For the MRI exams, you will lie down on a narrow bed which will then be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will need to lie there quietly for about 1/2 hour, during which time there will be a loud banging noise. You may feel warm during this procedure. You will be asked to hold your breath for up to 25 seconds, several times. The instrument to conduct this

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measurement is located at University of California Davis Medical Center, and a member of the study team will drive you there.

24-hour blood drawing with catheter: On study days 4 and 20, you will have an intravenous line placed by a Registered Nurse in a vein in your forearm for drawing blood samples. A needle will be inserted into a vein in your arm through which a small, flexible plastic tubing (catheter) is placed into your vein. The needle will be removed leaving the tubing taped in place. This tubing will allow us to collect several small blood samples in one day without multiple venous punctures. We will collect 32 samples at 30-60 minute intervals starting at 8:00 AM when you are fasting and ending at 8AM the next morning. During this period breakfast will be provided at 9:00 AM, lunch at 1:00 PM, dinner at 6:00 PM. Each meal needs to be consumed within 30 minutes, prior to the next blood draw. Most of the blood samples collected will consist of approximately 1 tsp, but the 3 samples collected before breakfast and 3 of the samples collected after dinner will consist of 2 or 3 tsp. If we are unable to collect all samples because the catheter does not work, we will collect up to five single-tube samples throughout the course of the test day using individual vein punctures. We will measure the level of sugar, fat, and a number of hormones in these samples. We will also collect and save the white blood cells from these samples in order to conduct DNA analysis.

- **Oral Glucose Tolerance and Disposal Test (OGTDT):** Two times we will perform an OGTDT. These tests will occur immediately after the end of the 24-hour blood collection, on Study Days 5 and 21. Following the final 24-hour blood draw at 8AM, you will drink 11 ounces of a glucose solution. It will be necessary that you drink all the glucose solution within 5 minutes. Some of the glucose in the solution will be labeled with a nonradioactive isotope. Your blood will be sampled again 30, 60, 90, 120, 180 and 240 minutes later. You will not consume food during this 4-hour period and you will be limited to one cup of water. Each sample collected during the OGTDT will be approximately ½-1 teaspoon. The total amount of blood collected during the 18 day study will be approximately 2 ¼ cups.
- **Total body water measurement:** We will measure the amount of water in your body by bioimpedance spectroscopy. Electrodes will be placed your hand, foot, ankle and wrist. This measurement will take less than 5 minutes. It will occur immediately before each OGTDT.
- **Urine Collection:** On Study Days 3, 18, 19, you will be asked to provide 4 urine samples (before each meal and after dinner). If you are participating in the room calorimeter studies you will collect all urine you pass throughout each stay in the calorimeter.
- **Physical Measurements:** Your height, waist, and hip circumference will be measured at the beginning and end of the study. Body weight will be measured before breakfast each day during

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inpatient days. Your blood pressure will be measured routinely during inpatient study (2 times/day) using a standard blood pressure cuff.

- **Physical Activity questionnaire:** On Study Day 18 you will be asked to fill out a questionnaire about your physical activity during the prior 2 weeks.

Outpatient procedures:

- **24-hour Food Recall:** The Study Registered Dietitian will telephone you on 3 different days to ask questions about the food that you consumed the day before. These phone interviews are approximately 30 minutes long and will occur at the times that you specify as most convenient for you.
- **Beverage Pick-up:** On Study Days 9 and 13, you will report to the CCRC to pick up a new supply of sugar-sweetened beverages. Body weight and blood pressure will be measured, and a urine samples will be collected for measurement of the biomarker during these visits. The visit on Study Day 13 will be scheduled in the morning to allow collection of the fasting blood sample and measurement of breath hydrogen in response to sugar beverage consumption (described below). If you fail to keep your appointment for sugar beverage pickup and do not make other arrangements in time to allow for uninterrupted beverage consumption as required by the protocol, you will be dismissed from the study for non-compliance.
- **1 Week Intervention Fasting Blood Draw and Hydrogen Breath Test:** On Study Day 13 (a beverage-pickup day), a fasting blood sample (1/2 tsp) will be collected by venipuncture. Afterwards, the hydrogen breath test will be administered. Prior to the test we will provide you with antiseptic mouth wash in order that you can clean your mouth. You will then breathe into a breath collection bag. You will drink 12-16 ounces of sugar-sweetened beverage. Thirty, 60, 90 and 120 minutes later, you will again breathe into breath collection bags. To ensure the validity of these tests, on the day before (Study Day 12) you will not consume alcoholic beverages and you will eat a low fiber diet. You will also not eat or drink anything except water before these tests, starting at 8PM the night before.

Study Completion: When all the above procedures have been performed, the study will be completed. A clinical chemistry, lipid and blood profile will be performed on a blood sample collected on study day 20. The results will be reviewed by the Study Physician to determine that all the values are normal or they have not changed negatively compared to values measured before the study.

Study location: Most of the study procedures will be done at the CCRC at Mather Hospital. The MRI scans are performed at the Radiology Department of UCDCMC. The 23-hour metabolic rate monitoring will occur in the Whole-Room Calorimeter located in the WHNRC Building at UC Davis.

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DRS Daily Study Schedule

| Day | What you do |
|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Screening Day | Get routine blood tests, Medical history, Physical Activity questionnaire, Hydrogen breath test. |
| Study Day 1 | (If selected) Metabolic rate monitoring in whole-room calorimeter at WHNRC. Check in at 7AM, start at 8AM, out 7AM next day, energy balance meals. |
| Study Day 2 Monday | Sunday night before—fast starting at 8PM. Inpatient day: Arrive at CCRC at 7AM for check-in, physical examination. Fasting blood draw, heparin infusion, postheparin blood draw, buffet-style meals with appetite assessment. DEXA scan, BW/BP/Waist/Hip/Height. |
| Study Day 3 Tuesday | Inpatient day: Fat biopsies 8AM and 8PM. BW/BP, Urine collection, energy balance meals, UCDMC Hepatic/ Abdominal MRIs, heparin infusion, postprandial blood draw, heparin infusion, postheparin blood draw |
| Study Day 4 Wednesday | Inpatient day: BW/BP, Start 24-hour blood collection--8AM. |
| Study Day 5 Thursday | End 24-hour blood collection--8AM. BW/BP, Total body water measurement, Start OGTD--8AM, end--12PM. Lunch with sugar beverage/CCRC check-out with sugar beverage supply. Start drinking one sugar beverage with meals, 3 times/day. |
| Study Day 6 Friday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. |
| Study Day 7 Saturday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. |
| Study Day 8 Sunday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Provide 24-hour food recall information to Registered Dietitian during scheduled phone call. |
| Study Day 9 Monday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Pick up sugar beverages at CCRC, BW/BP/Urine Collection. |
| Study Day 10 Tuesday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. |
| Study Day 11 Wednesday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Provide 24-hour food recall information to Registered Dietitian during scheduled phone call. |
| Study Day 12 Thursday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Fast starting at 8PM |
| Study Day 13 Friday | Fast in morning: Fasting Blood Draw, Hydrogen Breath Test at CCRC, BW/BP/Urine Collection. Pick up sugar beverages at CCRC. Drink one sugar |

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| | beverage with each meal, 3 times/day. |
| Study Day 14 Saturday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. |
| Study Day 15 Sunday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. |
| Study Day 16 Monday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Provide 24-hour food recall information to Registered Dietitian during scheduled phone call. |
| Study Day 17 Tuesday | Outpatient day: Drink one sugar beverage with each meal, 3 times/day. Fast starting at 8PM. |
| Study Day 18 Wednesday | Inpatient day: Arrive at CCRC at 7AM for check-in, physical examination. Fasting blood draw, heparin infusion, postheparin blood draw, urine collection, buffet-style meals with appetite assessment. BW/BP/Waist/Hip/Height. Physical activity questionnaire |
| Study Day 19 Thursday | Inpatient day: BW/BP, Fat biopsies 8AM and 8PM. Urine collection, energy balance meals, UCDMC Hepatic/ Abdominal MRIs, postprandial blood draw, heparin infusion, postheparin blood draw |
| Study Day 20 Friday | Inpatient day: BW/BP, Start 24-hour blood collection--8AM. |
| Study Day 21 Saturday | Inpatient day: End 24-hour blood collection--8AM. BW/BP, Total body water measurement, Start OGTD--8AM, end--12PM. Lunch/Snack. Study complete for subjects not participating in metabolic rate monitoring. For subjects participating in metabolic rate monitoring, lunch with sugar beverage. CCRC check-out with sugar beverage supply. Continue drinking one sugar beverage with each meal, 3 times/day, until 2 nd whole-room calorimeter monitoring is complete. |
| Study Day 22a,b,c,d Sunday, Monday, Tuesday, Wednesday | Drink one sugar beverage with meals, 3 times/day until Study Day 23. |
| Study Day 23 Mon or Tues or Wed or Thurs | Metabolic rate monitoring in whole-room calorimeter at WHNRC. Start 8AM, out 7AM the next day, energy balance meals. Submaximal walking treadmill test. End of study. |

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POTENTIAL RISKS AND DISCOMFORTS

You may have adverse events or discomforts while taking part in this research study. While on the study, you are at risk for these side effects. Everyone taking part in the study will be watched carefully for any side effects. You should discuss these with the researcher and/or your regular doctor. However, the Investigator does not know all the side effects that may happen. These may occur at the time of procedure or later. We would expect all side effects caused by drink the sugar-sweetened beverages to go away shortly after consumption of the beverages are stopped, but in some cases, there could be side effects that can be serious or long lasting or permanent. Risks and side effects related to the procedures and the consumption of the sugars we are studying include:

Likely

- **Diet:** You may have to eat when you are not feeling hungry, or you may feel hungry and you won't be able to eat at that time. You may experience indigestion, nausea or changes in your bowel function due to the diet and/or changes in your normal eating habits. If you do experience significant and uncomfortable symptoms, medications such as Colace, Imodium, Gas-X or Pepto Bismol may be used as needed. You may experience feelings of shakiness, irritability, sweating, fatigue, nausea, and hunger after drinking the sugar beverage alone without solid food. These reactions can usually be avoided by consuming the sugar beverage along with meals. You may have to eat some foods and beverages that you do not like very much. If you routinely drink caffeinated coffee, you may experience headaches due to caffeine withdrawal. Consumption of the KoolAid beverages may cause your urine to appear dark yellow, or greenish yellow.
- **Body weight change:** It is possible that the diet may cause changes in weight. Following completion of the study, any such changes should return to normal on a healthy meal plan such as the USDA Food Pyramid. Dietary guidelines will be provided at the end of the study.
- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.
- **Fat Biopsies:** There may be pain similar to a bee sting during the injection of anesthetic prior to the fat biopsies. The needle biopsies are performed when the area is numbed and there is usually minimal or no discomfort. After the anesthetic wears off, the area may be sore for about a week. Bruising can occur at the site of biopsies. In order to minimize the amount of bruising and pain, the biopsies will be performed by a Physician or Nurse Practitioner with experience in taking biopsies from human subjects.
- **Catheter:** Sometimes proper insertion of the catheter is not accomplished on the first attempt and additional insertion attempts are necessary. You have the option of requesting that no more

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insertion attempts be made. During pre-screening, the nurses will assess your vein to evaluate the likelihood that the catheters can be inserted successfully for the multiple blood draw procedures. The nurses will need to flush the catheter line with saline solution in order to be able to draw blood. It is possible that flushing the catheter line with saline solution may cause some discomfort at the area where the catheter is inserted. Sometimes a successfully inserted catheter line stops working later during the long blood 24-hour blood collection procedure. The nurse will try to prevent this from happening by placing a heating pad on your arm. If the catheter line does stop working, the nurse will insert a new catheter. You have the option of requesting that a new line not be inserted. In this case we will collect up to five more samples throughout the remaining test period using a needle and syringe.

- **24-h blood collection:** You may become bored and tired during the long blood collection procedures, where your activity and mobility will be limited due to the infusion lines. There is a moderate risk that you will become irritable, fatigued, anxious or nauseated. The blood sampling which will occur during the night is done as unobtrusively as possible, but it still likely that this will interfere with your ability to experience uninterrupted sleep. We recommend that you bring from home movies and books and any other activities that will help you to pass the time more pleasantly. The CCRC has a small library of movies that are also available for you to watch. There are some people whose personalities are not suited to the limited mobility and activity required during the long blood collection procedures. Please carefully consider your ability to undergo these all day and night blood collection procedures.
- **Whole-room calorimeter 23-hour metabolic rate monitoring:** You may become bored or tired during the long metabolic rate monitoring procedure while you are confined to the whole-room calorimeter. The room is equipped with DVD Player, and internet hookup.
- **Submaximal treadmill test:** During this test your respiration rate and heart rate will increase, and you will be asked the work to a 'hard' level of exertion, so that you will be sweating and may feel 'out of breath' by the end of this procedure. There is also a possibility of muscle soreness during the three days following this test, particularly if you are not used to regular exercise.
- **Anemia:** We will collect the amount of blood during the 23-day study that is collected during a blood donation. The loss of red blood cells, also called anemia, can cause tiredness, weakness and shortness of breath.
- **Oral Glucose Tolerance and Disposal Test:** You may experience symptoms such as hunger, shakiness and sweating during the final hour of the Oral Glucose Tolerance and Disposal Test. These symptoms will be quickly alleviated by the lunch or snack that is provided immediately following the completion of test.

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Principal Investigator: Peter J. Havel

Less Likely

- **Lipid changes:** It is possible that the diet may cause changes in cholesterol and triglyceride levels, or blood pressure. Following completion of the study, any such changes should return to normal on a healthy meal plan such as the USDA Food Pyramid. Dietary guidelines will be provided at the end of the study. If analysis of your blood samples collected at the end of the study shows significant unfavorable changes, we will request that you come back for another blood draw in approximately a month. If lipid levels are still high, a dietitian will be available to assist you with an appropriate eating plan. You also may be referred to your physician for lipid-lowering therapy.
- **Fat biopsies:** Infection can occur at the site of biopsies.
- **Radiation (x-ray) risks:** As a result of participating in this study, you will receive a significant amount of radiation. The amount is similar to that received in many standard x-ray procedures, but is far more than you would receive from natural daily exposure, and carries at least a theoretical risk. If you are especially concerned with radiation exposure, you should discuss this with the researchers.
- **CT scan risks:** CT scans involve the risks of radiation (see above). Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time.
- **MRI risks:** Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which could in the process possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear ear plugs. At times during the test, you may be asked to not swallow for a while, or to hold your breath for 25 seconds, which can be uncomfortable.

Because the risks to a fetus from MRI are unknown, pregnant women cannot participate in this study.

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- **Submaximal treadmill test:** While walking on the treadmill certain changes are possible, including fainting, irregular heartbeat, extreme elevations of blood pressure, and, in rare instances, heart attack or death. We have greatly minimized this risk by choosing a submaximal test that predicts aerobic capacity, rather than performing a maximal test. Further, additional measures to minimize these risks include an evaluation of risk factors obtained during the screening process, including your blood lipid values, blood pressure, history of tobacco use, and family medical history, and monitoring your blood pressure and heart rate during testing. Emergency equipment and trained personnel are available onsite to deal with unusual situations that may arise.

EXPECTED BENEFITS

There will be no direct benefit to you from participating in this study. However, this study will help scientist learn more about the effects of drinking sugar-sweetened beverages, and it is hoped that this information will help to further knowledge about diet and health.

OTHER OPTIONS TO TAKING PART IN THIS STUDY

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. You may want to talk to your doctor before deciding if you will take part in this study.

RIGHT TO WITHDRAW FROM THE STUDY

Taking part in this study is your choice. You can decide to stop at any time.

If you choose not to take part in this study, you will not be penalized or lose any benefits to which you are entitled. Your decision will not affect your relationship with the researcher.

Tell the Investigator if you are thinking about stopping or decide to stop.

The investigators will terminate the participation of particular subjects who are unable or unwilling to comply with drinking the sugar-sweetened beverages, or who display uncooperative, aggressive or rude behavior during procedures or during inpatient stays at the CCRC.

CONFIDENTIALITY

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law.

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We will disclose your information if it is necessary to protect your rights or welfare. For example, you are injured and are in need of emergency care. We will disclose your information if the researcher becomes aware that you may be a danger to yourself or to others. We will disclose your information if the researcher becomes aware that acts of child, elder, or dependent adult abuse or neglect may have occurred. If information from the study is published or presented at scientific meeting, your name and other personal information will not be used.

Once you have been identified as a research participant, you will be assigned a random number, which will be used as the study identification code. This identifier will be used in all data spreadsheets and reports to the Principal Investigators and statisticians. The key to the identifiers, as well as the consent forms with your name, research data, and related records will be protected from inappropriate disclosure and will be stored in a locked cabinet. We protect the medical information data on the computer with passwords. This prevents access by other unauthorized staff.

The research sponsor, the National Institute of Health may also look at your research files and study related medical record.

The Institutional Review Board at UC Davis and the Research and Development Committee at VANCHCS whose purposes are to review, approve, and monitor research studies, which involve human subjects, also have the authority to review all research records for quality assurance.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

VA policy requires that if you are a VA patient, a note be placed in your medical record that identifies you as taking part in this research.

RESEARCH RELATED INJURY

Diagnosis and treatment may be for routine care or for research. Some forms of diagnosis and treatment involve some risk of injury.

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If you are injured as a result of being in this study, treatment will be available. If you are eligible for veteran's benefits, the costs of such treatment will be covered by the Department of Veterans Affairs. If not, the costs of such treatment may be covered by the Department of Veterans Affairs or the University of California, depending on a number of factors. The Department of Veterans Affairs and the University do not normally provide any other form of compensation for injury. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form. For further information about this, you may call the V.A. District counsel at 415-750-2288 or the office of the UC Davis Institutional Review Board Administration at 916-703-9151.

COSTS TO STUDY SUBJECTS

There is no charge for you to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the sponsor/department excepting the expense of travel to the CCRC. It is estimated that you will need to make at least 5 trips to the CCRC. No other expenses to you are anticipated, with the exception that the inpatient days will require time away from work for subjects with jobs (about 8 days). The food served at the CCRC and the sugar-sweetened beverages are provided at no cost to you.

PAYMENT FOR TAKING PART IN THE STUDY

In return for your time, effort and travel expenses, you will be paid for taking part in this study. The total compensation will be \$1020 you complete the study, but did not participate in the RMR. The total compensation will be \$1180-1230 if you complete study and also participated in the RMR. The exact amount is dependent on the number of interim days that you must continue to consume the sugar-sweetened beverages between Study Day 21 and Study Day 23. If you do not complete the study, you will be compensated for the days completed. If you do not complete an entire Oral Glucose Tolerance and Disposal Test, 24-Hour Blood Collection procedure, or 23-hour RMR monitoring, you will be compensated for each hour of participation. These payments will be available as a check from the University of California, Davis within 4 weeks of study completion.

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DRS Study Schedule w/ Compensation

| Study day | Weekday | Inpatient/Outpatient status | Procedures | Compensation (\$) RMR Non-participant | Compensation (\$) RMR Participant |
|---------------|---------|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|-----------------------------------|
| 1 | Mon | Inpatient- WHNRC | Whole-Room Calorimeter - in 8AM, out 7AM next day | 0 | 75 |
| 1 | Tues | Inpatient- WHNRC | | | |
| 1 | Wed | Inpatient- WHNRC | | | |
| 1 | Thur | Inpatient- WHNRC | | | |
| 1 | Fri | Inpatient- WHNRC | | | |
| | Sat | | | | |
| | Sun | | | | |
| 2 | Mon | Inpatient/Check-in 7:00h | Pre-Postheparin Blood fast, BW/BP, Waist/hip/height, Buffet meals/Appetite assessment, DEXA, Physical activity recall questionnaire | 75 | 75 |
| 3 | Tues | Inpatient | BW/BP, Fat biopsies 8AM/8PM; Urine collection; UCDCMC Hepatic/Abdominal MRI; Pre-Postheparin blood draw 8PM | 75 | 75 |
| 4 | Wed | Inpatient | BW/BP, 24hr blood collection | 150 | 150 |
| 5 | Thur | Inpatient/Checkout 14:30PM | BW/BP, OGTTD/lunch with first sugar drink | 100 | 100 |
| 6 | Fri | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 7 | Sat | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 8 | Sun | Outpatient | Sugar beverage with each meal, 3/day; 24-hr food recall | 10 | 10 |
| 9 | Mon | Outpatient | Sugar beverage with each meal, 3/day; Beverage pickup/Urine collection | 20 | 20 |
| 10 | Tues | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 11 | Wed | Outpatient | Sugar beverage with each meal, 3/day; 24-hr food recall | 10 | 10 |
| 12 | Thur | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 13 | Fri | Outpatient | Beverage pickup, urine collect, fast blood collect, hydrogen breath test, Sugar beverage with each meal, 3/day | 40 | 40 |
| 14 | Sat | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 15 | Sun | Outpatient | Sugar beverage with each meal, 3/day, 24-hr food recall | 10 | 10 |
| 16 | Mon | Outpatient | Sugar beverage with each meal, 3/day | 10 | 10 |
| 17 | Tues | Outpatient | Sugar beverage with each meal, 3/day; Fast starting 8PM | 10 | 10 |
| 18 | Wed | Inpatient/Check-in 7:00h | Pre-Postheparin Blood fast, BW/Waist/hip, urine collection Buffet meals/Appetite assessment, Physical activity recall questionnaire | 75 | 75 |
| 19 | Thur | Inpatient | BW/BP, Fat biopsies 8AM/8PM; urine collection, UCDCMC Hepatic/Abdominal MRI/Pre-Postheparin Blood 8PM | 75 | 75 |
| 20 | Fri | Inpatient | BW/BP, 24-hr blood collection | 150 | 200 |
| 21 | Sat | Inpatient/Checkout 14:30PM | BW/BP, OGTTD/lunch with sugar drink (or end of study) | 100 | 100 |
| 22 | Sun | Outpatient | | Study complete | 10 |
| 23 | Mon | Inpatient- WHNRC | Whole-Room Calorimeter - in 8AM, out 7AM next day, Snack, submaximal walking treadmill test | | 75 |
| 23 | Tues | Inpatient- WHNRC | | | |
| 23 | Wed | Inpatient- WHNRC | | | |
| 23 | Thur | Inpatient- WHNRC | | | |
| 23 | Fri | Inpatient- WHNRC | | | |
| | | | | | 10 |
| | | | | | Study complete |
| Totals | | | | 1020 | 1190-1230 |

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POSSIBLE COMMERCIAL PRODUCTS

Samples taken during this study may be used for research and development purposes not related to your treatment or condition. You will not have any property rights or ownership interest in products or data which may be derived from your samples.

By consenting to take part in this study, you authorize the use of your bodily fluids. The blood or urine samples obtained from you will become the property of Dr. Peter Havel. Once you have provided the specimens, you will not have access to them. These will be used only for this research study. The use of your sample may result in inventions or discoveries that could become the basis for new procedures or diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value and may be patented and licensed. Commercially available products may be developed from these samples. There are no plans to share any of these profits with you.

FUTURE USE OF SPECIMENS

During the screening visit and the course of research, the investigator will remove some blood and urine. We would like to keep some of the blood and urine that is left for future research purposes. Your specimen(s) will only be used for research purposes. If you agree, these specimen(s) will be kept and used to learn more about diet and metabolism.

The research that may be done with your specimen(s) will not benefit you directly nor have an effect on your care. It might help people in the future. Any reports about the research, done with your specimen(s), will not be shared with you or your doctor and the reports will not be put in your health record.

Your name, address, phone number and any other identifying information will be taken off anything associated with your specimen before it is given to the researcher. This would make it very difficult for any research results to be linked to you or your family. Also, people outside the research process will not have access to results about any one person which will help to protect your privacy.

The benefits of research using specimens include learning more about what causes diseases, how to prevent them, how to treat them, and how to cure them. There are very few risks to you. The greatest risk is the release of information from your health records which may be necessary for us to obtain along with your specimens. We will protect your records so that your name, address, and phone number will be kept private.

Please read each question below and think about your choice. After reading each question, initial next to "YES" or "NO". If you have any questions, please discuss this with the researcher.

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1. My tissue may be kept for use in future research: YES _____ NO _____
2. Someone may contact me in the future to ask me to take part in more research: YES _____ NO _____

For further information on the use of specimens for future research purposes and your rights as a research participant, please visit: <http://research.ucdavis.edu/IRBAdmin/Participants> .

QUESTIONS ABOUT RESEARCH SUBJECT RIGHTS

You can talk to the Investigator about any questions or concerns you have about this study at:

___ Dr. Peter Havel _____ at phone number ___ 530-752-3114 _____

___ Kimber Stanhope _____ at phone number ___ 530-752-6553 _____

___ Dr. Andrew Bremer _____ at phone number ___ 916-734-7098 _____

For questions about your rights while taking part in this study contact the UCD Institutional Review Board Administration or the VANCHCS Human Research Protection Program. You may call the UCD Institutional Review Board Administration at (916) 703-9151 or write to the Institutional Review Board, CTSC Building, Suite 1400, Rm. 1429, 2921 Stockton Blvd., Sacramento, CA 95817. The IRB Administration office will inform the Institutional Review Board which is a group of people who review the research to protect your rights. The IRB Administration office has also developed a web site designed to make you familiar with your rights. The web site discusses your basic rights as a research participant, an explanation of the informed consent process, basic requirement that written consent be in a language understandable to you, and suggested sample questions to ask the research investigator regarding your participation in the study. This web site can be accessed at:

www.research.ucdavis.edu/IRBAdmin .

To contact the VANCHCS Human Research Protection Program, please call (916) 366-5359 or you may also call the VA Regional Counsel at (415) 750-2288.

Name of Participant:

Date:

Title of Study: CCRC: The Metabolic Effects of Consuming Sugar-Sweetened Beverages for Two Weeks

Principal Investigator: Peter J. Havel

RESEARCH SUBJECT'S RIGHTS:

I have read or have had read to me all of the above.

Kimber Stanhope _____ has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call Dr.

Bremer _____ at 916-734-7098 _____ during the day and Dr. Bremer _____ at 916-762-6959 _____ after hours. If any medical problems occur in connection with this study the VA will provide emergency care.

I understand my rights as a research subject, and I voluntarily consent to participate in this study. I understand what the study is about and how and why it is being done. I will receive a signed copy of this consent form.

Subject's Signature

Date

Signature of Subject's Representative*

Subject's Representative

Signature of Witness

Witness (print)

Signature of Investigator

*Only required if subject not competent.

Participant's Initials _____