STUDY CONSENT FORM: The effects of orange juice compared with sugar-sweetened beverage on risk factors and metabolic processes associated with the development of cardiovascular disease and type 2 diabetes

APPROVAL DATE: 11-15-2022

NCT number: 03527277

Principal Investigator: Kimber Stanhope

Permission to Take Part in a Human Research Study

Title of research study:

The effects of orange juice compared with sugar-sweetened beverage on risk factors and metabolic processes associated with the development of cardiovascular disease and type 2 diabetes

Investigator: Kimber Stanhope, Ph.D.

Co-Investigator: Jean-Marc Schwarz, Ph.D.

Why am I being invited to take part in a research study?

We invite you to take part in a research 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 and you are between the ages of 18-50 years. You have reported a stable body weight during the prior 6 months and routinely consume 3 meals per day.

What should I know about a research study?

(Experimental Subject's Bill of Rights)

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**
- If you agree to take part, you will be given a copy of this document. Who can I talk to?

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at

Kimber Stanhope:	***530-752-3720 (office)***
	530-219-0914 (cell)
Study Staff:	***530-752-2714 (office)***
	530-752-2146 (office)
Dr. Valentina Medici:	***916-734-3751 (office)***
	916-919-1665 (cell)
Dr. Jay Shubrook:	***707-638-5970 (office)***

Do not write below this line. For IRB stamp and version date only.

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For non-emergency and after-hour issues you can call or text Kimber Stanhope, the Principal Investigator (530-219-0914). For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to Valentina Medici. In the case of an emergency, dial 911 from any phone.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/policiescompliance/irb-admin/.You may talk to an IRB staff member at (916) 703-9151, hs-irbadmin@ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

This research is being conducted by the research group of Dr. Kimber Stanhope, Ph.D., R.D. in the Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis (UC Davis) and Jean-Marc Schwarz, Ph.D. (Touro University, CA) and funded by National Institute of Health. The main goal of a research study is to learn things to help patients in the future. No one can guarantee that a research study will help you.

We hope to learn more about the effects of consuming sugar-sweetened beverages or orange juice with meals in a situation in which we know exactly what the other meal components consists of. Therefore, throughout the entire study we will provide the participants with either sugar-sweetened beverages or orange juice and the meals that they will consume with the beverages. This will allow us to compare the effects that sugar-sweetened beverages or orange juice have on your blood triglyceride and cholesterol concentrations and your body's sensitivity to the hormone insulin without having to account for the other components in your usual diet.

How long will the research last?

We expect that you will be in this research study for approximately 40-47 days. It may exceed 47 days if schedule adjustments have to be made to accommodate unforeseen problems.

How many people will be studied?

We expect to enroll about 72 participants.

What happens if I say yes, I want to be in this research?

BEFORE YOU BEGIN THE STUDY

This study requires all COVID-19 safety procedures to be followed by subjects and study staff. In order to comply with UC Davis campus policies, anyone coming onto campus (student, employee or visitor) is required to follow the COVID-19 safety guidelines which can be found at this website: https://campusready.ucdavis.edu/. Safety requirements may include filling out the UC Davis Daily Symptom Survey during each campus visit and participating in COVID-19 tests. Additionally, you will be required to wear a mask during study interactions, temperature will be taken at each visit and 6-feet distancing must be maintained during all interactions with staff, excepting the Registered Nurses. For

transport by study staff in UCD vehicles to study procedure sites, you will be provided and required to wear a KN-95 or N-95 mask, face shield and to sit 6 feet away from the driver and any other passenger.

You will be asked to have the following "screening" exams, tests or procedures to find out if you can be in the study.

- UC Davis pre-screening survey (either via telephone or online using Qualtrics) to determine if you meet the basic body weight and health requirements to participate in the study. If your survey responses indicate that you may qualify for participation in this study, staff will contact you to set up an online screening interview.
- Online screening interview to determine if you wish to consent to participate in this study. This involves the following activities and questionnaires.
    - **Questionnaires**: You will be asked to fill out a questionnaire about your medical history, general physical activity and usual diet at home. Female participants will be asked to provide information regarding the date of their last menstrual period and forms of contraception.
    - **Commitment to study diet**: You will be asked to view the breakfast, lunch and dinner study menus and describe your ability and willingness to commit to eating these food items and only these food items throughout the entire 6 weeks of the study. You may request and arrange to pick up meal samples for taste-testing.
    - **Commitment to participating in time-consuming experimental procedures:** You will be asked to describe your availability and willingness to participate in experimental procedures (described elsewhere in this document) that require you to spend an all-day period (approximately 14 hours including transport time) at the beginning of the study and again, 4 weeks later, at the Touro University Metabolic Research Center (TMRC, 1310 Club Drive, Vallejo, CA). You will be shown a calendar of study dates, and asked to indicate the dates that you will be available to participate. You will also be asked to describe your availability and willingness to participate in the other experimental procedures (described elsewhere in this document) that include a magnetic resonance imaging (MRI) procedure that will occur at 7:00 AM at the University of California, Davis Medical Center (UCDMC, Sacramento, CA) at the beginning of the study and again, 4 weeks later. You will also be asked to collect all your urine over a 24-hour period three times during the study, and collect a stool sample two times during the study. Participation in this study will also require that you report to University of California, Davis at the Ragle Human Nutrition Research Center (HNRC) (or in the foyer outside the entrance) two times each week to pick up the study meals and/or beverages that will be consumed throughout the duration of the study and to return empty and not-empty food packaging. The commitments are detailed in **Table 1: Study schedule with procedures, timing and compensation**

If you can commit to the study diet and procedures and sign this consent electronically using DocuSign, we will make an appointment for you to visit one of our study clinics for blood tests that will determine your eligibility. The test will occur at either the UC Davis Health System Laboratory Patient Service Center (2660 W. Covell Blvd, Davis); the main campus of University of California, Davis at the Ragle Human Nutrition Research Center (Ragle HNRC) 1283 Academic Surge); or at the University of California, Davis Medical Center (UCDMC) Clinical and Translational Science Center Research Center (CCRC) (located off of Stockton Blvd. in Sacramento). At the clinic you will be asked to give a fasted 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. A follow up draw may be requested if necessary to determine eligibility.

For the blood 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 for 12 hours before your scheduled appointment time at the lab.

Preparation for study participation: If the screening exams, tests or procedures show that you can be in the study, and you choose and are selected to take part, there may be a considerable waiting period before the study will actually start. During this period the following will occur:

- 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.
- Marijuana use is not allowed during this study. In order to be eligible to participate in this study, you must be willing to forego all marijuana use for 5 weeks before the study and throughout the study.
- You will be asked to confirm your availability and willingness to participate by responding to emails 3 weeks and a few days before your study start date.
- At approximately 2 weeks before the study begins, we will ask you to come to Ragle HNRC or the foyer outside of Ragle HNRC so we may measure your height and body weight and provide you with a body weight scale. You will be asked to weigh yourself on the scale each morning before you dress or eat or drink. You will provide us with these weights via phone call or text each day and we will use that data to determine the amount of diet we will provide you. You will continue to provide us with daily weights throughout the study to help us provide you the accurate amount of diet to ensure stable body weight.
- Female participants will be asked to take a urine preganancy test during the scale pick up visit. Because some of the experimental procedures may affect a fetus, and because pregnancy can affect the study results, pregnant individuals may not participate in this study. A urine pregnancy test will also be done prior to procedures (DEXAs and MRIs) that may affect a fetus to ensure negative pregnancy results.

DURING THE STUDY

When the study starts, you will participate in the following dietary protocol, tests and procedures (also shown in ***Table 1: Study Procedures: Schedule, Duration & Compensation***):

DIETARY PROTOCOL:

- **Standardized diet**:
  - You will be restricted to eating only the study food provided during the entire 6 weeks of the study. You will be restricted from eating outside non-study foods. You will be served a standardized diet consisting of a breakfast, lunch, dinner and snack and you will need to adhere to this diet plan. The amount of food provided is based on your calculated energy requirement. This is a standard calculation used for all subjects, so it is important to report to the study staff if you feel that you are being provided with too much or too little food. There will be specific meals provided to you the day before or day of a scheduled procedure that must be eaten in full. This is necessary in order for this study to produce scientifically accurate information. If giving up all of your favorite foods and drinks for 6 weeks is something that you are not willing to do, this study is not suitable for you.
- **Sugar-sweetened or naturally-sweetened beverages**:

- You will be restricted to drinking only water, black coffee (if applicable) and the study beverages provided during the entire 6 weeks of the study. You will be restricted from drinking outside beverages, including alcohol (except water and black coffee).
- **Intervention**: Upon completion of all the initial baseline procedures, for the last 4 weeks of the study, you will drink sweetened beverages. These beverages will be provided to you as 3 servings/day, approximately 12-16 fluid ounces/serving, and are to be consumed one at each meal.
- You will be provided with beverages that contain either sugar or orange juice.
- In order for this study to produce scientifically useful information, it is necessary that you consume all 3 of the beverages provided each day for the last 4 weeks of the study.
- The sweetened beverage that you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what beverage you get. You will have a one in two chance of being given a sugar-sweetened beverage.

- **Beverage and Meal Pick-up/Return:** During appointments scheduled at your convenience, you will report to Ragle HNRC or to the foyer outside of Ragle HNRC two times/week to pick up a 3- or 4-day supply of meals/snacks/beverages, and to return uneaten food and packaging. Your temperature will be measured using a contactless thermometer. You will be asked to provide a urine sample in a urine collection cup using the restroom in the foyer area. All exchanges of meal & beverage tote bags, study collection supplies, and samples will be conducted with both you and study staff member wearing masks and maintaining a 6-foot distance. Thus, there will be a designated cart or area to exchange items for turn-in and pick-up. The cart or area will also have a supply of sterile wipes and disposable gloves so all items can be decontaminated prior to being picked up. If you fail to keep your appointments for study meal and beverage pick-up/return and do not make other arrangements in time to allow for uninterrupted study diet consumption as required by the protocol, you will be dismissed from the study for non-compliance.

  Most study diet report forms, physical activity questionnaires and food surveys will be made available for you to complete electronically. The diet report forms are used to assess diet palatability and quantity, and describe diet deviations. You will fill out these reports daily and they will be reviewed by the Study Coordinator. Communication via text, email or a Zoom call will be used to discuss issues or request clarifications as needed.

  The purpose of the urine sample is to monitor compliance to the dietary protocol. Some of the diet components will contain a biomarker that can be measured in urine to confirm that the study beverages and study meals are being consumed. Urine will also be used to measure for evidence of alcohol consumption.

TESTS AND PROCEDURES AT UCD AND UCDMC: These tests will occur during the baseline (first 2 weeks of the study when study beverages are not consumed) and intervention period (the last 4 weeks of the study when study beverages are consumed).

- **24-hour urine collection**: Three times during the study (during the 2nd week of baseline, 2nd week of intervention and 4th week of intervention) you will collect all urine over a 24-hour period. You will be provided with pre-labeled bottles (enough to ensure all urine can be collected) containing a preservative solution in a designated ice chest with enough cold packs to maintain refrigeration temperatures. Each urine collection period will begin with the first collection occurring upon waking in the morning (no later than 9:00 AM) and end at approximately 9:00 AM the next

day. Upon completion of each collection, the bottles of urine will be transported to our laboratory in the designated ice chest by either yourself or our study staff.

- **MRI of abdomen and liver**: Two times during the study, you will come to the UCDMC Department of Radiology, Ellison Building, to have a fasting Magnetic Resonance Imaging (MRI) exam at 7:00-8:30 AM. Study staff can provide you transportation in a university vehicle or offer transportation using a rideshare service (i.e., Uber, Lyft, etc.). If due to the pandemic, you prefer to drive yourself, you will be reimbursed at the UCD mileage reimbursement rate. If you are driving yourself, a commucation schedule that will include a wake-up call if needed will be set up between you and the study staff to ensure you will arrive at the Ellison Building on schedule.
  The purpose of this exam is to measure the amount of fat in your liver and the fat volume within and outside of your abdominal cavity. For the MRI exams, you will lie down on a narrow bed that 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 up to 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. Female participants will also be asked to provide urine samples for a urine pregnancy test before each MRI procedure.
- **Stool collection**: Two times during the study, you will be asked to provide stool samples to test the effects of the sweetened beverages on the types of microorganisms contained in the stool. You will receive instructions and a sample collection kit that contains ice packs, labeled sample vials, a fecal collection kit, zip-lock bags, and sealable secondary container freezer bag. You will collect feces in a disposable fecal collection vessel that attaches to the toilet. You will then transfer two separate portions of the sample into two separate sample vials using the spoons attached to the vial tops. Each vial will be placed into the provided zip-lock bag and then into the secondary freezer bag with ice packs. The secondary freezer bag with samples inside should be frozen immediately after collection. Samples will be returned at your next scheduled meal/beverage pick-up visit.
- **Fasting blood draw:** During the final week of the study, usually following the second MRI exam, you will have a fasting blood draw that will be used for the same laboratory tests performed at screening. These end of study results will be compared with the screening results. The test will occur at either the UC Davis Health System Laboratory Patient Service Center (2660 W. Covell Blvd, Davis); the main campus of University of California, Davis at the Ragle Human Nutrition Research Center (Ragle HNRC); or at the University of California, Davis Medical Center (UCDMC) Clinical and Translational Science Center Research Center (CCRC) (located off of Stockton Blvd. in Sacramento).

TESTS AND PROCEDURES AT TOURO UNIVERSITY METABOLIC RESEARCH CENTER (TMRC):

The tests described below will be conducted two times during the study during a 14-hour visit (includes transport time) to TMRC.

- **Isotope consumption for measurement of fat production in the liver:** You will be provided with two doses of an oral stable-isotope (1-^{13}C acetate) that will be consumed at 8:00 PM and 11:00 PM the night before the visit to the TMRC. A third dose of isotope will be provided and consumed at 6:30-7:00 AM the next morning. Three more doses will be consumed at the TMRC; at 9:00 AM and with meals at 12:00 PM and 4:00 PM. Each oral dose of the isotope will consist of 1-2 grams 1-^{13}C acetate in approximately 4-8 ounces of water. The isotope allows liver fat production to be measured in the blood samples that will be collected every 30-60 minutes from 8:45 AM to 8:00 PM.
- **Transport to TMRC:** Study staff will provide you transportation to TMRC (50 miles away from UCD) in a university vehicle or offer transportation using a rideshare service (i.e., Uber, Lyft, etc.). It will be necessary to leave Davis at 6:45 AM in order to ensure arrival at the TMRC by 8:00 AM in heavy traffic conditions. If due to the pandemic, you prefer to drive yourself, you will be reimbursed at the

UCD mileage reimbursement rate. If you are driving yourself, a commucation schedule that will include a wake-up call if needed will be set up between you and the study staff to ensure you will arrive at TMRC by 8:00 AM.

- **Blood pressure:** Blood pressure will be measured after arrival at the TMRC, and at least 2 more times during the day. Weight, height, waist and hip measurements will be taken.
- **Blood collection procedures:** At 8:15-8:30 AM you will have an intravenous line placed in a vein in your forearm by a Registered Nurse. 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 blood samples every 30 or 60 minutes, starting at 8:45 AM and ending at 8:00 PM, without multiple venous punctures. The time of each collection and the amount of blood collected at each timepoint is shown in **Table 2**. 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 12-hour period using individual vein punctures.
- **Urine Collection**: A urine sample will be collected before 9:00 AM and after consumption of lunch and dinner.
- **Oral glucose tolerance test (OGTT) for measurement of insulin action:** Following the 9:00 AM blood collection, you will drink 75 grams of glucose in approximately 11 ounces of water. The blood samples will be collected every 30 minutes for the next 3 hours and will be used to determine how quickly insulin clears glucose from your blood.
- **Lunch:** Lunch will be provided at 12:00 PM.
- **Diet questionnaires:** You will be asked to complete some questionnaires related to eating and food.
- **%Body fat**: We will measure the composition of your body (lean, fat, mineral) 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. If the DEXA scanner at TMRC is not available, the DEXA scan will be performed at the CCRC. A urine pregnancy test will be performed on a urine sample from female participants prior to the DEXA procedure.
- **Dinner:** Dinner will be provided at 4:00 PM and will need to be consumed before the 4:30 PM blood draw.
- **Post-meal blood changes:** The blood samples collected from 12:00 PM to 8:00 PM will allow us to measure your before- and after-meal levels of glucose, insulin, fat and hormones. We will also collect and save the white blood cells from these samples in order to conduct DNA analysis.

Table 1: Study Procedures: Schedule, Duration & Compensation

Week	Procedure	Location	Time	Details	Compensation
Baseline ~ 2 weeks		**Energy-balanced baseline diet**			
-2	*Scale Pick-up*	*Ragle HNRC*	*TBD by subject*	*2 weeks before study start; scale pick-up visit*	$10
-2 - 6	*Fasting BW*	*Home*	*pre-breakfast*	*Text, email or phone in fasting BW daily*	$65
0	Study Overview	Home	TBD by subject	Zoom meeting for study/schedule review & questions	$10
0	1st Meal Pick-up	Ragle	TBD by subject	1st meal pick-up visit	$10
1 - 2	Diet	Home/ Ragle	TBD by subject	Consume study meals each day Pick-up/dropoff for study meals; urine collection: 2 times/week	$40
1	MRI #1	UCDMC Radiology	7:00 AM	MRI	$50
1	Stool Collection #1	Home	TBD by subject	Stool collection	$20
2	24-h UC #1	Home	TBD by subject	24 hour urine collection	$30
2	Pre-TMRC Evening	Home	8:00 &11:00 PM	Consume oral isotope	$40
2	TMRC Visit #1	TMRC	7:00 AM	Transport to TMRC, Consume oral isotope	$150
			8:00 AM	Check-in, vitals & measurements, start catheter	
			8:45 AM	Start blood collection every 30 or 60 minutes	
			9:00 AM - 12:00 PM	Oral glucose tolerance test	
			12:00 PM	Lunch, Consume oral isotope	
			1:00 - 3:00 PM	Study questionnaires, DEXA scan	
			4:00 PM	Dinner, Consume oral isotope	
			8:00 PM	Final blood draw, remove catheter, check-out	
Intervention ~ 4 weeks		**Energy-balanced intervention diet & study beverage**			
3-6	Diet	Home/ Ragle	TBD by subject	Consume study meals & beverages each day Pick-up/dropoff for study meals/beverages; urine collection: 2 times/week	$140
3	24-h UC #2	Home	TBD by subject	24 hour urine collection	$40
5	Stool Collection #2	Home	TBD by subject	Stool collection	$20
6	24-h UC #3	Home	TBD by subject	24 hour urine collection	$50
6	MRI #2	UCDMC Radiology	7:00 AM	MRI	$50
6	Pre-TMRC Evening	Home	8:00 &11:00 PM	Consume oral isotope	$45
6	TMRC Visit #2	TMRC	7:00 AM	Transport to TMRC; Consume oral isotope	$200
			8:00 AM	Check-in, vitals & measurements, start catheter	
			8:45 AM	Start blood collection every 30 or 60 minutes	
			9:00 AM - 12:00 PM	Oral glucose tolerance test	
			12:00 PM	Lunch, Consume oral isotope	
			1:00 - 3:00 PM	Study questionnaires, DEXA scan	
			4:00 PM	Dinner, Consume oral isotope	
			8:00 PM	Final blood draw, remove catheter, check-out	
End of Study					
				TOTAL	**$970**
Procedure days are approximate and dependent on clinic and subject availability (baseline visits will occur in the first 2 weeks of the study and intervention visits will occur between the 5th and 6th week of the study)					

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Table 2: Blood Collection Times & Volume

Scheduled time of draw	TMRC visit 1 (baseline) blood draws (cc / tsp)	TMRC visit 2 (intervention) blood draws (cc / tsp)	EXIT study blood draw (cc / tsp)
8:00			6 cc or ~1.3 tsp
8:30	27 cc or ~ 5.5 tsp	27 cc or ~ 5.5 tsp	
9:00	27 cc or ~ 5.5 tsp	27 cc or ~ 5.5 tsp	
9:30	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
10:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
0:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
11:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
11:30	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
12:00	17 cc or ~3.5 tsp	17 cc or ~3.5 tsp	
13:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
14:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
15:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
16:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
16:30	8 cc or ~1.7 tsp	8 cc or ~1.7 tsp	
17:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
17:30	4 cc or ~0.9 tsp	4 cc or ~0.9 tsp	
18:00	13 cc or ~ 2.7 tsp	13 cc or ~ 2.7 tsp	
19:00	23 cc or ~4.7 tsp	23 cc or ~4.7 tsp	
20:00	23 cc or ~4.7 tsp	23 cc or ~4.7 tsp	
Total	*272 cc or ~9.2 ounces*	*272 cc or ~9.2 ounces*	*6 cc or ~1.3 tsp*
Total blood volume for study			**550 cc or ~18.6 ounces**

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

- Following all UC Davis COVID-19 safety guidelines including COVID-19 testing and completetion of the UC Davis Daily Symptom Survey during each campus visit.
- Providing accurate assessment regarding potential COVID-19 exposure and symptoms.
- Consuming only the study meals/snacks provided and not any outside food as required for ~6 weeks
- Consuming the 3 study beverages per day as required for ~4 weeks
- Consuming only the study beverages provided and not any other sweetened beverages
- Picking up new supplies of the study beverages and meals 2 times per week
- Returning all empty and not empty food packaging/containers at each next visit
- Reporting any deviations from the dietary protocol to the Study Coordinator
- Participating in the study procedures
- All provided study supplies and materials are property of the University of California, Davis and it is your responsibility to return them upon completion of study

What happens if I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you.

Is there any way being in this study could be bad for me?

WHAT SIDE EFFECTS OR RISKS CAN I EXPECT FROM BEING IN THE STUDY?

You may have side effects while on this study. Everyone taking part in the study will be watched carefully for any side effects. However, the Researcher may not know all the side effects or risks. Side effects may be mild or very serious. The Researchers may give you medicines to help lessen side effects. Many side effects go away soon after you stop consuming the sugar-sweetened beverages. In some cases, side effects can be serious, long lasting, or may never go away. You should talk to the Researchers about any side effects that you have while taking part in the study. Risks and side effects related to the procedures and the consumption of the sugars we are studying include:

- **Diet**:
    - During the entire 6 weeks of the study, you will be restricted to eating only the study meals provided. You may want to eat or drink other things and you will not be able to eat or drink them (with the exception of water and black coffee) during this time. We ask you to consider carefully whether this restriction is one that you can accommodate. If your lifestyle includes many social situations that are centered on eating and drinking, this restriction may be particularly difficult. It could also be difficult if you strongly prefer your accustomed foods over any other foods. You may have to eat some foods and beverages that you do not like very much or at all. All study meal items are available to be taste-tested before you commit to this study.
    - There may be times when you have to eat when you are not feeling hungry, or there may be times when you 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 Tums, Colace, Gas-X or Pepto Bismol may be used as needed.
    - Consumption of the study diet/beverages may cause your urine to appear dark yellow, or greenish yellow.
- **Lipid changes**: It is possible that consumption of the sugar-sweetened beverages will cause your cholesterol (including low density lipoprotein-cholesterol (LDL-C)) or triglyceride concentrations to increase above the normal risk range. Elevated concentrations of LDL-C are associated with increased risk for cardiovascular disease, including coronary artery disease. Following completion of the study, any such changes should return to normal on a healthy meal plan such as the USDA MyPlate. 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, you may 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.
- **Acetate isotope consumption:** The acetate isotope that will be consumed is naturally-occurring and non-radioactive. Acetate is the main ingredient in vinegar, thus the isotope dose might have a slight vinegar or salty flavor.
- **Blood drawing risks**: Drawing blood and insertion of the catheter by venipuncture will cause temporary discomfort from the needle stick. Drawing blood may cause bruising. In rare instances, drawing blood may cause infection.

- **Catheter**: Sometimes proper insertion of the catheter is not accomplished on the first attempt and additional insertion attempts are necessary. 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 long blood collection procedures. 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 may request that prior to doing so, that the nurse review other options. If most of the essential blood samples have been collected, collecting the remaining essential samples at 7:00 PM and 8:00 PM using a needle and syringe may be an option. The other option may be to end your participation in the study.
- **Blood collection procedures**: You may become bored and tired during the day-long blood collection procedures, where your activity and mobility will be limited. There are televsions in the patient rooms, but we recommend that you bring your laptop, books and any other activities from home that will help you to pass the time more pleasantly. 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 procedures.
- **Anemia**: Blood drawing results in fewer red blood cells. The loss of too many red blood cells is called anemia, and can cause tiredness, weakness and shortness of breath. To minimize this possibility, the amount of blood that will be collected is within generally accepted guidelines for drawing blood from research subjects and the combined total collected is equivalent to the amount of blood provided in a single blood donation.
- **Oral glucose tolerance test**: Consumption of the oral glucose solution may cause symptoms of high blood sugar, which include an increase in your need to urinate or increase in thirst; or symptoms of low blood sugar which include blurred vision, shakiness, nausea, headache, fatigue, rapid heart rate, or being more easily annoyed. If any symptoms occur, your blood glucose will be measured immediately. If it is determined that the symptoms are the result of a blood glucose level that is too low, you will be provided with glucose tablets to consume, followed by a snack and lunch.
- **Radiological risks (DEXA scan)**: This study involves a low radiation exposure that is less than other diagnostic tests using ionizing radiation. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.
- **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 potentially 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 eligible to participate in the study. 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. You should not be or become pregnant while on this research study. We will conduct a urine pregnancy test before each MRI exam.
- In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be severe.
- The research may also hurt a pregnancy or fetus in ways that are unknown. You should not be or become pregnant while on this research study.

Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include generating study results that will have a positive impact on public health.

What happens to the information collected for the research?

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study. The Accounts Payable Department will also view your personal information (social security number and address) for payment processing.

The sponsor, monitors, auditors, the IRB will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your research records may be looked at by the sponsor of this study and government agencies or other groups associated with the study.

If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your EMR until the study is complete to ensure that the study remains unbiased. If necessary for your care, this information will be provided to you or your physician.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/legal/privacy/) and in an attached document.

The PI has received a Certificate of Confidentiality from the Federal government that will help protect the privacy of the research records. The Certificate of Confidentiality allows the Researchers to refuse to disclose identifying information on your participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself and your involvement in this research. If you have given your consent for an insurer or employer to obtain information about you, the Researcher may not use the Certificate of Confidentiality to withhold this information. A Certificate of Confidentiality also does not prevent a Researcher from disclosing information about you to prevent serious harm to yourself or others, such as reporting to the authorities' incidents of child abuse, elder abuse or spousal abuse.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include noncompliance in regards to eating and drinking the study meals and beverages provided, failure to show up for scheduled meal and beverage pick-up appointments or experimental procedures, evidence that non-study foods are being consumed (e.g., excessive weight gain) or unexplained weight loss.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

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.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at HS-IRBAdmin@ucdavis.edu.

If you agree to take part in this research study, we will compensate you $970 for your time and effort. This amount may be greater if scheduling adjustments result in your remaining in the study for longer than 47 days from the first day of study meal consumption. Beyond 47 days, we will compensate $10/day for each additional day you are consuming the study diet and an additional $15 for any extra diet pick-up visits. If you do not complete the study, you will receive a prorated payment based on the number of study days completed (see Table 1 from page 8). Payments for TMRC inpatient Study Days will be prorated based on the number of hours completed out of a maximum of 14 hours (~2 hours travel time, ~12 hours at clinic). This is in addition to the mileage reimbursements if you provide your own transportation to UCDMC or TMRC. This amount is calculated as the UCD mileage reimbursement rate for 44 miles to and from UCDMC and for 100 miles to and from TMRC. Payment forms will be processed when your participation in the study has ended. There will be no compensation for participation in screening or consenting procedures. You will receive a 1099 from the University for tax reporting purposes. You may be asked for your social security number for payment purposes. It will not be used for any other purpose without your permission.

Bio-specimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

Upon completion of participation, the results that will be shared with you include body weight, waist and hip measurements, copies of your clinical blood tests which are generated from the blood samples

collected during screenings and during final week of study and DEXA scans. Other study results will not be shared with you, as they will generally be unavailable until the end of the 5-year study.

Are there other research opportunities?

If you are interested in being contacted for future research, please provide your phone number and/or email. This is completely optional.

_____(initials) Yes, I am willing to be contacted for future research opportunities. My phone number and/or email is: _____.

Do not write below this line. For IRB stamp and version date only.

APPROVED by the Institutional Review Board at the University of California, Davis	
Protocol	APPROVED
1167030	November 15, 2022

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

Do not write below this line. For IRB stamp and version date only.

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