Cardiometabolic Effects of Pecans as a Snack
NCT05071807
April 22, 2022

CONSENT FOR RESEARCH

The Pennsylvania State University

Title of Project: Cardiometabolic effects of including pecans as a snack to improve diet quality: a randomized controlled study

Principal Investigator:

Name: Dr. Kristina Petersen
Address: 303 Chandlee Lab,
University Park 16802
Telephone: 814-865-7206

Subject's Printed Name: _____

We are asking you to be in a research study. This form gives you information about the research.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is listed later in this form. If you have any questions, be sure to ask the study team.

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

We invite you to take part in a research study because you meet our age, BMI, smoking, and medication requirements and are free of heart disease, stroke, kidney or liver disease.

What is the purpose of this research study?

The purpose of this voluntary research study is to study how including 2 oz./day of pecans in your diet or continuing your current diet affects risk factors for heart disease and diabetes.

How long will the research study last?

This study will last 12 weeks.
Screening appointment:
Day 1: Forms, blood pressure, weight, height, waist circumference, blood draw – 45-60 minutes
(pregnancy testing: females only – 5 minutes)

Beginning of treatment period:
Day 1: blood draw, weight, waist circumference, vascular testing– 60 minutes
(pregnancy testing: females only – 5 minutes)
Consume meal that is provided for your dinner/supper meal

Day 2: blood draw, FMD – 45 minutes

End of treatment period (week 12):
Day 1: blood draw, weight, waist circumference, vascular testing– 45 minutes
(pregnancy testing: females only – 5 minutes)
Consume meal that is provided for your dinner/supper meal

Day 2: blood draw, vascular testing – 45 minutes

Picking up food/gift card and compliance tracking sheet questionnaires and calls, fecal collections, and completing 24-hour diet recalls: ~ 7 hours

Total time for clinic and diet center visits from the beginning to the end of the study ~12 hours

What will you need to do?
For this study, you will be asked to attend clinic visits (blood vessel measures and blood draws), provide fecal samples, pick up study foods/gift cards and complete compliance tracking sheets, and complete 9 dietary records.

What are the main risks of taking part in the study?
For this study, the main risks to know about are:

-Allergic reaction to pecans; cross contamination of study foods
-Bruising and discomfort from heart health measures
-Pain, discomfort, lightheadedness or dizziness may occur from blood draw
-Embarrassment with fecal collection kit
-Loss of confidentiality

What are the possible benefits to you that may reasonably be expected from being in the research?
There are no benefits to you from taking part in this research. Results of the study may benefit other people in the future by helping us learn more about the role of pecans in management of heart disease and metabolic risk.

What happens if you do not want to be in this research?
You may choose not to take part in this research study.

1. **Why is this research study being done?**

We are asking you to participate in this research to study how including 2 oz./day of pecans in your diet or continuing your current diet affects risk factors for heart disease and diabetes. We will be measuring the effect on heart health, blood pressure, blood cholesterol and glucose levels, and gut health.

This research is being done because approximately 50% of Americans are at risk for heart disease and diabetes and therefore strategies are needed to lower risk. Pecans are a nutrient rich food that may help to reduce the risk of these diseases. However, studies to date have not examined the effect of incorporating pecans in the diet on diet quality and risk factors for heart disease and diabetes.

Approximately 128 people will take part in this research study conducted at the Pennsylvania State University, University Park Campus, PA.

2. **What will happen in this research study?**

General overview of the study

If you agree to participate in this study, your participation will last approximately 12 weeks in total. In this study, participants will be allocated to one of two groups. The allocations will be made randomly, similar to tossing a coin. If you are in group 1, you will be provided with two ounces of pecans per day and be asked to consume this in place of the snacks that you usually consume for the entire 12-week period. The pecans will be provided by the research team. If you are in group 2, you will be asked to continue eating your usual diet and make no changes during the 12-week period. You will be given $30 worth of gift cards per month, which is equal to the value of the pecans group 1 will receive. Regardless of whether you are in group 1 or 2, you are required to come to campus monthly to receive the pecans or gift cards and to complete questionnaires. You will also receive biweekly compliance phone calls. Throughout the entire study we will ask that you do not consume peanuts or tree nuts other than the ones we give you. This is not a weight loss study, so you must try to keep your body weight and physical activity level constant throughout the entire study.

Procedures to be followed

Screening:

This visit will consist of filling out forms (medical history, personal information); measuring height and weight so that body mass index (BMI) can be calculated; measuring waist circumference, and blood pressure to determine eligibility. A blood sample will be taken from a forearm or hand vein and a complete blood count, including liver and kidney function and a blood fat panel will be performed (approximately 19 ml of blood or 1.25 tablespoons will be taken). You will feel a small pinch or discomfort when the needle is inserted. If the initial blood draw is unsuccessful it may need to be repeated, with your permission. If you take thyroid medicine, and do not have a current lab test (within 6 months), we will draw 3.5 ml (0.2 Tbsp) more blood to conduct a thyroid test. If you are female of child bearing potential, you will be given a urine pregnancy test. You will be contacted within 3-5 days with the results of the screening blood sample. A clinician at the CRC will review all of the screening data and based on this the research team will determine your eligibility. If you are eligible for the study, you will be contacted to schedule your start date and baseline data collection appointments. There will be no charge for the screening blood work or measurements. You will receive these results. If you agree to continue your participation in this study, you will agree to check with the study staff before participating in any other research studies; the study coordinator will determine if you can participate.

Baseline and endpoint testing

At the beginning and end of the study (12-weeks) you will have your weight and waist circumference measured. If you are female of childbearing potential, you will be given a urine pregnancy test.

Blood sampling:

You cannot consume any food or drinks except for water for 12 hours, and cannot drink alcohol during the 48 hours prior to having your blood taken.

In addition to the blood taken at screening, blood samples will also be taken on two consecutive days at the beginning and end of the study (12-weeks). After a 12 hour fast (consumption of no food or drink except water), a blood sample will be taken from your arm. If the initial blood draw is unsuccessful it may need to be repeated, with your permission. Approximately 60 ml (about 4 tablespoons) of blood will be collected over the two days of testing (30 ml or 2 tablespoons each day). Therefore, over the ~12-week study, blood will be taken 4 times with a total amount of approximately 120 ml (8 tablespoons). A typical American Red Cross blood donation is 1 pint (473 ml). Blood samples will be frozen and analyzed at the end of the study (when all of subjects have completed the study). The results of the study will only be available at the end of

the study (which may take up to 3 years). Your blood may be tested for the following: blood fats (total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides), blood sugar (glucose, fructosamine, HbA1c), insulin, and markers of inflammation or other measures related to risk for heart disease or diabetes. No personal information will be kept with any sample – only ID# assignments – and only the Primary Investigator, co-investigator and study personnel will have access to the ID# assignments with the study files.

Measures of vascular (heart) health:

Flow mediated Dilation:
Pre-menopausal women will be scheduled for testing within 7 days of starting their menstrual period to control for hormonal effects on vascular function.

At the beginning and end of the study (12-weeks) you will undergo a test that determines the health of your arteries. This test will be performed using an ultrasound machine.

Ultrasound is often used to see images of babies in the womb. We will use ultrasound to measure the diameter of an artery in your upper arm, before and after the inflation of a blood pressure cuff on the forearm. In most people, this procedure produces dilation (opening up) of the artery.
Ultrasound will be used to collect images of the brachial artery in your right arm. This procedure is known as Flow Mediated Dilation (FMD). The FMD test takes about 30 minutes and is performed as follows:

1. In a private room, you may be asked to remove your shirt and put on a hospital gown. (You will not be asked to remove any clothing below the waist). You will lie quietly on a bed in a quiet, darkened room.
2. Your right arm will be extended at a 45-degree angle from your shoulder and rest on some foam cushion supports. A blood pressure cuff will be placed on your forearm.
3. A research assistant will place 3 EKG electrodes (stickers) on your upper chest and stomach.
4. You will be asked to rest for 5 minutes.
5. A technician, trained in medical ultrasound, will sit at the head of the bed. The technician will apply ultrasound gel on your arm and will place an ultrasound probe (which looks like a microphone) on that arm.
6. An image of the blood vessels in your arm will be viewed on the ultrasound equipment next to the bed. The technician may need to move the probe over a small area of your upper arm to obtain the clearest image. The image of the artery will be videotaped for 1 minutes.
7. Next, the blood pressure cuff on your lower arm will be tightly inflated (to a pressure of 250 mmHg) and it will remain inflated for 5 minutes.
8. While the cuff remains inflated, the technician will continue to record the image of the artery in your upper arm. At the end of 5 minutes, the cuff will be deflated and images will be captured and recorded for an additional 2 minutes. It is very important throughout the recording that you rest quietly and keep your arm as still as possible.

Pulse wave analysis (PWA) and Pulse Wave Velocity (PWV):
You will undergo a test that measures your blood pressure and pulse wave forms at the beginning and end of the study (12-weeks). The PWA measurement is very similar to a routine blood pressure measurement. Prior to the measurement, you will be asked to sit quietly with your feet flat on the floor for at least 5 minutes. A blood pressure cuff will be placed on your upper arm. The cuff will inflate, then deflate for 5 seconds, and then partially re-inflate. It is important that you remain still during this measurement. The procedure will be repeated twice, for a total of 3 measurements. Repeated measurements are used to increase accuracy. For the PWV measurement, we will ask you to lay flat on a hospital bed without a pillow. A blood pressure cuff will be placed on your upper leg. We will gently place a hand-held sensor against an artery in your neck. This will measure the pressure waves of the blood in your artery. Once a good waveform

is obtained, the blood pressure cuff on your leg will inflate to measure the pressure waveforms in that artery. Having these simultaneous measurements allows the device to calculate the speed at which blood is traveling through your arteries. The PWV test will also be performed three times.

Fecal collection:
At the beginning and end of the study (12-weeks) you will be asked to collect a fecal sample (~50 g). You will be provided with a stool sample kit and detailed instructions for collection of a clean sample at home. The samples will be stored for possible future analysis of amount and number of different bacteria in your stool samples as a measure of your gut microbiome.

Dietary intake:
You will be asked to complete three, 24-hour dietary recalls at the beginning of the study, in week 6 of the study and in week 12 of the study; a total of 9 recalls. You will complete these recalls using an online system (Automated Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool) at home or at the Clinical Research Center. Study staff will provide you with a login code and you will be asked to provide information about the foods, beverages, and supplements you consumed during the previous day. These will be completed at home.

Monthly Metabolic Diet Center Visits:
At the end of your second day of baseline testing, you will be asked to go to the Metabolic Diet Center to collect your study food or gift card as well as a compliance sheet. You will be asked to fill this sheet out daily and adhere to the instructions provided. These meetings will be coordinated through the Diet Center Manager Marcella Smith: 814-863-9745 (office) 814-280-0136 (cell).

3. What are the risks and possible discomforts from being in this research study?

Dietary intervention
You will be asked to report any food allergies during the telephone screening, however, it is possible that an unknown food allergy may manifest during the study. This is most likely to occur within the first week of the study since the pecans will be eaten daily. It is unlikely that you will experience any discomfort with the addition of pecans. However, you may have an unknown sensitivity to this amount of pecans that may cause you to experience GI (stomach) upset such as bloating, diarrhea, or gas. You should report any adverse reactions to study personnel.

Food preparation
The pecans will be handled according to accepted standards of sanitation and provisions are made to ensure the safety of the pecans provided for off-site consumption. However, it is possible that incorrect food handling during shipping, storage or preparation, if not detected, could result in food-borne illness. Every effort will be made to safeguard against this possibility. To date, no food related contamination or illnesses have occurred.

Blood Sampling
Blood draws often cause mild pain, swelling or bleeding. There may be some bruising (blood under the surface of the skin), which will be minimized by pressing on the site after the needle is removed. There is also a slight chance of infection, dizziness or fainting. These risks will be minimized and most likely eliminated by having trained nursing staff draw the blood in a clinical setting using sterile supplies. If dizziness or fainting occurs, the symptoms will be alleviated by having you lie flat with your feet raised. The nursing staff will ask that you remain at the clinic until your blood pressure has been checked and you are cleared from any further risk.

Vascular Ultrasound Test (FMD)
There are no known risks associated with ultrasound. However, because the blood pressure cuff on your right forearm is inflated tightly, it is likely that your hand and arm below the blood pressure cuff will experience "pins and needles" (tingling and pricking) sensations while the cuff is inflated and for a few minutes after it is released. This feeling is similar to what you feel when your hand or foot "falls asleep." During the 5 minutes that the blood pressure cuff is inflated on your forearm, your arm could become numb and we will ask you not to move it. This might be moderately painful. However, any discomfort or numbness should go away within minutes of cuff deflation and there are no known long-term risks associated with this test. There is a possibility for red blotching or mild bruising (petechiae) to appear on the skin above and below the location of the blood pressure cuff. Studies indicate that petechiae are rare (occurring in less than ½ of 1% of patients) and it is typically not uncomfortable and it does not require treatment. There are no risks associated with measurement of blood pressure, heart rate, or EKG as long as you are not allergic to adhesive tape. Temporary redness at the site of the electrode placement is possible.

All recordings from the ultrasound will have no personal identifying information associated with them and will be stored in a secure, password-protected folder only accessible by approved study personnel.

Pulse Wave Analysis (PWA) and Pulse Wave Velocity
There are no known risks associated with these measurements. There will be a sensation of pressure from the blood pressure cuff. There is a possibility for red blotching or mild bruising (petechiae) appearing on the skin above and below the location of the blood pressure cuff. Studies indicate that petechiae are rare and typically not uncomfortable and do not require treatment.

Loss of Confidentiality
There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

Stool collection
You may experience some level of embarrassment or discomfort from being asked to collect stool samples. However, you will be provided with detailed instructions on how to collect the samples within the comfort of your own home, and at your convenience, to help reduce any concerns you may have.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to you?
Participants will receive their screening laboratory results, including a complete blood count, interpretation of liver and kidney function, and blood lipid values, at no cost.

4b. What are the possible benefits to others?
The study may provide information related to the role of pecans in management of heart disease and metabolic disease risk factors.

5. What other options are available instead of being in this research study?
You may decide not to participate in this research.

6. How long will you take part in this research study?
The study period is approximately 12 weeks. Pre-menopausal women will be scheduled for testing within 7 days of starting their menstrual period to control for hormonal effects on vascular function.

You will be expected to go to the Metabolic Diet Center on campus monthly for compliance monitoring and provision of the pecans or gift card as well submission of a compliance tracking sheet. At the beginning of the study and at 12 weeks, endpoint data will be collected.

Total time for study visits, after the initial screening is approximately 4 hours. Times may vary and females will require an additional 5 minutes for a urine pregnancy test at baseline and the end of each diet period. The following is an estimate of the amount of time you will spend in study activities:

Screening appointment:
Day 1: Forms, blood pressure, weight, height, waist circumference, blood draw – 45-60 minutes (pregnancy testing: females only – 5 minutes)

Beginning of treatment period:
Day 1: blood draw, weight, waist circumference, vascular testing– 60 minutes
(pregnancy testing: females only – 5 minutes)
Day 2: blood draw, vascular testing– 45 minutes

End of treatment period (week 12):
Day 1: blood draw, weight, waist circumference, vascular testing– 60 minutes
(pregnancy testing: females only – 5 minutes)
Day 2: blood draw, vascular testing – 45 minutes

Picking up food/gift card and compliance questionnaires and compliance calls, fecal collections, and completing 24-hour diet recalls: ~ 7 hours

Total time for clinic and diet center visits from the beginning to the end of the study ~12 hours

7. How will your privacy and confidentiality be protected if you decide to take part in this research study?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information.

- An electronic list that matches your name with your code number will be saved in a secure, password-protected folder where only approved study personnel will have access.
- Your research records will be labeled with a unique ID number and will be kept locked at the PI's research office. All electronic records will be saved to a secure, password-protected folder only accessible by approved study personnel. All records associated with your participation in the study will be subject to the usual confidentiality standards applicable to medical records.
- Your research samples will be labeled with your unique ID number and will be stored in locked freezers at the CRC and in 318 Chandlee Lab. They will be maintained until three years after the date when the study is published, and then destroyed unless you give permission for us to keep your blood samples for future use (see end of document).

  For research specimens sent to other laboratories or facilities for analysis, no personal identifiable information will be used. Samples will be labelled only with ID numbers. Blood samples will be sent to LabCorp, Morrisville NC. Fecal samples will be sent to Wright Labs LLC, Huntingdon PA.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

We will do our best to keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may find out about your participation in this research study. For example, the following people/groups may check and copy records about this research.

- The Office for Human Research Protections in the U. S. Department of Health and Human Services
- U.S. Food and Drug Administration
- The research study sponsor, the American Pecan Council
- The Institutional Review Board (a committee that reviews and approves research studies) and
- Penn State's Office for Research Protections.

Some of these records could contain information that personally identifies you. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed.

7b. What will happen to my research information and/or samples after the study is completed?

In the optional portion of the consent form, we will ask for your permission to use or share your identifiable research information and blood and fecal samples with other investigators here or at other institutions. Future research may be similar to this study or completely different. You can be part of the current study without agreeing to the future use of your identifiable research information and your biological samples (blood and fecal).

8. What happens if you are injured as a result of taking part in this research study?

In the unlikely event you become injured as a result of your participation in this study, medical care is available. It is the policy of this institution to provide neither financial compensation nor free medical treatment for research-related injury. By signing this document, you are not waiving any rights that you have against The Pennsylvania State University for injury resulting from negligence of the University or its investigators.

9. Will you be paid or receive credit to take part in this research study?

For your participation in this study you will receive monetary compensation of $200, prorated as follows and paid at the end of your participation in the study. If you drop out of the study for any reason before its completion, the following compensation will be provided:

Completion of day 1 and day 2 testing at baseline = $50
Completion of three 24-hour recalls at baseline= $25
Completion of three 24-hour recalls at week 6 = $25
Completion of day 1 and day 2 testing at 12 weeks = $75
Completion of three 24-hour recalls at week 12 = $25

The total of $200 will be paid at the completion of the participant's involvement with the study.

If you are a Penn State employee, you will be asked to provide your name and Penn State ID number and payment will be provided by direct deposit via the payroll system. If you are not a Penn State employee, you will be paid by check and your Social Security Number must be collected for tax reporting purposes. The compensation that you receive for participation in this study is taxable income.

Total payments within one calendar year that exceed $600 will require the University to report these payments to the IRS annually. This may require you to claim the compensation that you receive for participation in this study as taxable income.

If determined that specific work or visa laws conflict, participants may not be eligible for compensation. Participants can discuss this with the research team for more information.

10. Who is paying for this research study?

The sponsor, the American Pecan Council is paying PSU for the research to be done.

11. What are your rights if you take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.
- If you stop being in the research, already collected data may not be removed from the study database.

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 non-compliance with the study protocol (consuming treatment foods) or study visits (attending clinic visits).

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If you have questions or concerns about this research study, whom should you call?

Please call the head of the research study (principal investigator), Dr. Kristina Petersen, at 814-865-7206if you:

- Have questions, complaints or concerns about the research, including questions about compensation.
- Believe you may have been harmed by being in the research study.

You may also contact the Office for Research Protections at (814) 865-1775, IRB-ORP@psu.edu if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints, or general questions about the research.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Office for Research Protections' website at https://www.research.psu.edu/irb/participants for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the ORP at (814) 865-1775.

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.

INFORMED CONSENT TO TAKE PART IN RESEARCH

Signature of Person Obtaining Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions the subject or subject representative has about the research.

_____	_____	_____
Signature of person obtaining consent	Date	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and agree to allow your information to be used and shared as described above.

_____	_____	_____
Signature of Subject	Date	Printed Name

Optional part(s) of the study
In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

Optional Storage of Tissue for Future Research
In the main part of this study, we are collecting blood samples and fecal samples from you. If you agree, the researchers would like to store leftover sample(s) for future research.

- These future studies may be helpful in understanding heart disease and diabetes.
- It is unlikely that these studies will have a direct benefit to you.
- Neither your doctor nor you will receive results of these future research tests, nor will the results be put in your health record.
- Sometimes tissue is used for genetic research about diseases that are passed on in families. Even if your samples are used for this kind of research, the results will not be put in your health record.

Your leftover samples will be labeled with a code number that will be linked to a master list accessible only to the PI, co-investigator and research team. This list will be destroyed 3 years after publication of the study results. These samples will be stored in a locked freezer in a locked office of the PI's.

- The length of time they will be used is unknown.
- You will be free to change your mind at any time before the master list is destroyed (approximately 3 years after publication of the study results) at which point we will no longer be able to identify your samples.
- You should contact the principal investigator if you wish to withdraw your permission for your blood samples or fecal samples to be used for future research. If it is still possible to identify your samples, any unused samples will be destroyed and not used for future research studies.

You should initial below to indicate what you want regarding the storage of your leftover blood samples and fecal samples for future research studies.

a. Your samples may be stored and used for future research studies to learn about diabetes and heart disease prevention.
_____Yes _____No

c. Your samples may be shared with other investigators/groups without any identifying information.
_____Yes _____No

Signature of Person Obtaining Consent

Your signature below means that you have explained the optional part(s) of the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____
Signature of person obtaining consent	Date	Printed Name

Signature of Subject

By signing below, you indicate that you have read the information written above and have indicated your choices for the optional part(s) of the research study.

_____	_____	_____
Signature of Subject	Date	Printed Name

Future Contact

Do we have permission to keep your personal information and contact you about your interest in participating in future studies for Dr. Petersen and her collaborators?

_____Yes _____No

Signature of Person Obtaining Consent

Your signature below means that you have explained the optional part(s) of the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____
Signature of person obtaining consent	Date	Printed Name

Signature of Subject

By signing below, you indicate that you have read the information written above and have indicated your choices for the optional part(s) of the research study.

_____	_____	_____
Signature of Subject	Date	Printed Name