HRP-591 - Protocol for Human Subject Research

Protocol Title:

Provide the full title of the study as listed in item 1 on the "Basic Information" page in CATS IRB (http://irb.psu.edu).

Glycemic effects of substituting pecans for snacks higher in saturated fat and added sugars in individuals with prediabetes

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Version Date:

Provide a version date for this document. This date must be updated each time this document is submitted to the IRB office with revisions. DO NOT revise the version date in the footer of this document.

4/3/26

Clinicaltrials.gov Registration #:

Provide the registration number for this study, if applicable. See "HRP-103- Investigator Manual", under "ClinicalTrials.gov" for more information.

NCT07235358

Important Instructions for Using This Protocol Template:

This template is provided to help investigators prepare a protocol that includes the necessary information needed by the IRB to determine whether a study meets all applicable criteria for approval.

1. **GENERAL INSTRUCTIONS[1]:**
   - Prior to completing this protocol, ensure that you are using the most recent version by verifying the protocol template version date in the footer of this document with the current version provided in the CATS IRB Library.
   - Do not change the protocol template version date located in the footer of this document.
   - Some of the items may not be applicable to all types of research. If an item is not applicable, please indicate as such or skip question(s) if indicated in any of the instructional text.
   - **GRAY INSTRUCTIONAL BOXES:** Type your protocol responses below the gray instructional boxes of guidance language. If the section or item is not applicable, indicate not applicable.
     - **Do NOT delete the instructional boxes from the final version of the protocol.**
   - **CHECKBOXES:** Either check the boxes or indicate an "X" before the checkbox. Do NOT delete checkboxes.
   - The protocol should be written in lay language. Do **NOT** copy and paste grant proposal information into the protocol.

[1] This template satisfies AAHRPP elements 1.7.B, I.8.B, I-9, II.2. A, II.2.I, II.3.A, II.3.B, II.3.C-II.3.C.1, II.3.D-F, II.4.A, III.1.C-F, II.2.D

- Add the completed protocol template to your study in CATS IRB (http://irb.psu.edu) on the "Basic Information" page.

2. **CATS IRB LIBRARY:**
   - Documents referenced in this protocol template (e.g., SOP's, Worksheets, Checklists, and Templates) can be accessed by clicking the Library link in CATS IRB (http://irb.psu.edu).

3. **PROTOCOL REVISIONS:**
   - When making revisions to this protocol as requested by the IRB, please follow the instructions outlined in the guides available in the Help Center in CATS IRB (http://irb.psu.edu) for using track changes.
   - Update the Version Date on page 1 each time this document is submitted to the IRB office with revisions.

If you need help:
Human Research Protection Program
Phone: 814-865-1775
Fax: 814-863-8699
Email: irb-orp@psu.edu
https://researchsupport.psu.edu/orp/irb/

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1.0 Objectives

1.1 Study Objectives

Describe the purpose, specific aims, or objectives. State the hypotheses to be tested.

The overarching goal of this study is to evaluate the glycemic and cardiovascular effects of substituting pecans for snacks higher in saturated fat and added sugars in individuals with prediabetes. To achieve this, a 16-week, 2-arm parallel, randomized controlled trial in adults with prediabetes will be conducted. Participants will be randomized to one of two groups: 1) provision of 1.5 oz/day of pecans with education to consume these instead of their currently consumed snacks higher in saturated fat and added sugars (intervention); 2) continuation of their habitual diet (control). The study aims to assess the effect of the intervention compared to the control on the following outcomes:

1. Markers of glycemic control, including hemoglobin A1C (HbA1C), fasting glucose, fasting insulin, homeostatic model of insulin resistance (HOMA-IR), lipoprotein insulin resistance index, mean glucose, time in range, glycemic variability, and insulin resistance.
2. Markers of cardiovascular health, including lipid/lipoprotein concentrations, lipoprotein particle size and concentrations, apolipoprotein B, blood pressure, C-reactive protein (CRP), and vascular health.
3. Dietary intake of saturated fat and added sugars, and overall diet quality.

It is hypothesized that replacement of usual snacks higher in saturated fat and added sugars with pecans will improve glycemic control, cardiovascular health, intake of saturated fat and added sugars, and overall diet quality compared to continuing usual intake after 16 weeks in adults with prediabetes. Therefore, this trial is expected to show that dietary substitution of commonly consumed unhealthy snacks with pecans improves blood sugar control and cardiovascular health thus potentially reducing disease risk. The results of the study are expected to inform dietary guidance about the types of snacks that can be included in healthy dietary patterns.

1.2 Primary Study Endpoints

State the primary endpoints to be measured in the study.

Research typically has a primary objective or endpoint. Additional objectives and endpoints are secondary. The endpoints (or outcomes), determined for each study subject, are the quantitative measurements required by the objectives. Measuring the selected endpoints is the goal of a trial (examples: response rate and survival).

Hemoglobin A1C (HbA1C)

1.3 Secondary Study Endpoints

State the secondary endpoints to be measured in the study.

Fasting glucose and insulin
Homeostatic model of insulin resistance (HOMA-IR)
Continuous glucose monitor (CGM) assessed mean glucose, time in range, and glycemic variability
Lipid/lipoprotein concentrations (triglycerides, total cholesterol, LDL-C, HDL-C, non-HDL-C)
Apolipoprotein B, lipoprotein particle size and concentration (LDL, HDL, triglyceride-rich lipoproteins)
Lipoprotein insulin resistance index
C-reactive protein
Central and peripheral blood pressure
Pulse wave velocity (PWV)
Saturated fat and added sugar intake

Overall diet quality, assessed by the Healthy Eating Index 2020

2.0 Background

2.1 Scientific Background and Gaps

Briefly describe the scientific background and gaps in current knowledge in lay language.

For clinical research studies being conducted at Penn State Health/Penn State College of Medicine, and for other non-PSH locations as applicable, describe the treatment/procedure that is considered standard of care (i.e., indicate how patients would be treated in non-investigational setting); and if applicable, indicate if the study procedure is available to patient without taking part in the study.

Approximately 38% of US adults have prediabetes.[1] Prediabetes is defined by the American Diabetes Association as a condition that precedes type 2 diabetes and is diagnosed by elevated HbA1C (5.7-6.4%), impaired fasting glucose (100-125 mg/dL), or impaired glucose tolerance assessed with a 75 g oral glucose tolerance test.[2] Individuals with prediabetes are at high risk for type 2 diabetes. For individuals with prediabetes at age 45 years, the lifetime risk of type 2 diabetes is 74%; the risk is higher for those with concomitant obesity.[3] In addition, prediabetes is associated with a heightened risk of cardiovascular disease (CVD).[2] Therefore, the goal of prediabetes management is to improve glycemic control to reduce the risk for progression to type 2 diabetes and the associated complications, including CVD risk.[2]

A key component of prediabetes management is intake of a healthy dietary pattern that emphasizes a variety of nutrient-dense foods to support glycemic control as well as cardiovascular health.[4] In the U.S., adherence to healthy dietary patterns is poor.[5] Therefore, strategies are needed to improve adherence to healthy dietary patterns.

In the U.S., snacks comprise ~20% of daily total energy intake[6]. While intake of nutrient-rich snacks is associated with better adherence to healthy dietary patterns, intake of snacks high in added sugars and saturated fat contributes to poorer adherence to healthy dietary patterns.[7,8] Therefore, replacing nutrient-poor snack foods with nutrient-dense alternatives may be a feasible strategy to improve adherence to healthy dietary patterns, which may assist with improving glycemic control and reducing CVD risk in individuals with prediabetes.

Nuts are a nutrient-dense food that are a recommended part of healthy dietary patterns[4,9,10] and nut intake is associated with better adherence to healthy dietary patterns.[8] Consistent evidence from epidemiological studies shows that higher nut intake is associated with lower risk of CVD.[11] This is supported by clinical trial evidence showing nut intake improves CVD risk factors, including low-density lipoprotein cholesterol (LDL-C), triglycerides[12,13], and glycemic control.[14,15] Prior clinical trials show pecans improve lipids and lipoproteins compared to non-nut comparators after 4-8 weeks[16–21].

2.2 Previous Data

Describe any relevant preliminary data.

In a randomized controlled trial conducted by the PI, it was demonstrated that instructions to eat 2 oz/day of pecans as a replacement for usual snacks improved LDL-cholesterol (-7.2 mg/dL; 95% CI -12.3, -2.1), non-HDL-cholesterol (-9.5 mg/dL; 95% CI -15.3, -3.7) and apolipoprotein B (-4.38 mg/dL; 95% CI -8.02, -0.73) after 12 weeks, compared with continuing usual intake, in adults at risk for cardiometabolic diseases.[20,21] We also observed an improvement in total LDL particles and total triglyceride-rich lipoprotein particles (TRL-P) as well as an improvement in the lipoprotein insulin resistance index, which is indicative of a reduction in early insulin resistance.[20,21] In addition, replacement of typical snacks with pecans increased overall diet quality, assessed by the Healthy Eating Index-2020 (a measure of adherence to the Dietary Guidelines for Americans), by 9.4 points (95% CI 5.0, 13.7) compared to the

usual diet group.[20] Collectively, this trial showed that instructions to replace all typical snacks with pecans for 12 weeks improved lipoproteins, early insulin resistance, and diet quality in people at risk for cardiometabolic diseases**.** Importantly, the lipid/lipoprotein, insulin resistance, and diet quality improvements observed with replacing all snacks with 2 oz/day of pecans were greater[20,21] than we have observed previously in studies examining the replacement of evening snacks only with peanuts (1 oz/day)[22] and pistachios (2 oz/day).[23] In these trials, replacing all snacks[20,21] or evening snacks only[22,23] with nuts did not consistently improve glycemic control, which is generally consistent with evidence on the glycemic effects of nuts.[14] However, previously replacement of snacks higher in saturated fat and added sugars with nuts has not been examined.

2.3 Study Rationale

Provide the scientific rationale for the research.

It is established that replacement of carbohydrates, including added sugars, and saturated fat with unsaturated fats improves glycemic control assessed by HbA1C. In a meta-analysis of 102 randomized controlled feeding trials, replacement of 5% of energy from carbohydrates with monounsaturated fatty acids (MUFA; -0.09%; 95% CI -0.12, -0.05) or polyunsaturated fatty acids (PUFA; -0.11%; 95% CI -0.17, -0.05) improved HbA1C.[24] Similarly, replacement of SFA with MUFA (-0.12; 95% CI -0.19, -0.05) or PUFA (-0.15; 95% CI -0.23, -0.06) reduced HbA1C.[24] More recently, in a 12-week randomized controlled trial in individuals with overweight or obesity, intake of 1 avocado per day lowered HbA1C by 0.06% after 12 weeks compared to a low-fat, higher carbohydrate food.[25] Thus, it is likely that education to consume pecans, which are low in carbohydrates and rich in unsaturated fats, instead of snacks higher in saturated fat and added sugars, will improve glycemic control, particularly in individuals with prediabetes defined by elevated HbA1C.

Therefore, this trial aims to evaluate the glycemic and cardiovascular effects of substituting pecans for snacks higher in saturated fat and added sugars, compared to continuing usual intake, in individuals with prediabetes. The intent of this study is not to evaluate pecans' ability to cure, mitigate, treat, or prevent disease. Rather, the intent is to see whether education to replace snacks higher in added sugars and saturated fat with pecans improves glycemic control and cardiovascular health, compared to continuing usual intake, in individuals with prediabetes. This evidence is expected to contribute to understanding the role of snacking in cardiometabolic health and inform dietary guidelines.

3.0 Inclusion and Exclusion Criteria

Create a numbered list below in sections 3.1 and 3.2 of criteria subjects must meet to be eligible for study enrollment (e.g., age, gender, diagnosis, etc.).

Vulnerable Populations:

You MAY NOT include members of these populations as subjects in your research unless you indicate this in your inclusion criteria because specific regulations apply to studies that involve vulnerable populations.
The checklists referenced below outline the determinations to be made by the IRB when reviewing research involving these populations. Review the checklists as these will help to inform your responses throughout the remainder of the protocol.

- **Children –**Review "HRP-416- Checklist - Children"
- **Pregnant Women** – Review "HRP-412- Checklist - Pregnant Women"
- **Adults with Impaired Decision-Making Capacity -** Review "HRP-417- Checklist - Adults with Impaired Decision-Making Capacity"

- **Prisoners-** Review "HRP-415- Checklist - Prisoners"
- **Neonates of uncertain viability or non-viable neonates-** Review "HRP-413- Checklist - Non-Viable Neonates" or "HRP-414- Checklist - Neonates of Uncertain Viability"

[Do not type here]

3.1 Inclusion Criteria

Create a numbered list of the inclusion criteria that define who will be included in your final study sample (e.g., age, gender, condition, etc.)

All the following inclusion criteria must be met at screening to be eligible for the study:

- Age 25-65 years
- Prediabetes assessed by an HbA1c of 5.7-6.4% at screening
- BMI 25-40 kg/m^2 at screening
- Low habitual nut consumption (<3.5 oz-eq/week) assessed at the telephone screening
- Regularly eats snacks higher in saturated fat and/or added sugars assessed at the telephone screening

3.1.1 Does this research involve collecting data from individuals residing outside of the US?

☒ No
☐ Yes – identify the countries where data collection will take place
[Type protocol text here]

3.2 Exclusion Criteria

Create a numbered list of the exclusion criteria that define who will be excluded in your study.

None of the following exclusion criteria must be met at screening to be eligible for the study:

- LDL-C ≥190 mg/dL at screening
- Hemoglobin <13.2 g/dL at screening
- Fasting triglycerides >350 mg/dL at screening
- ≥10% change in body weight within the 6 months prior to enrollment
- Blood pressure >140/90 mmHg at screening
- Type 1 or type 2 diabetes
- Prescription of anti-hypertensive, lipid-lowering, or glucose-lowering drugs
- Intake of supplements that affect the outcomes of interest (i.e., lipid, blood pressure, or glucose lowering; vitamin C or multi-vitamins containing vitamin C) and are unwilling to cease during the study period. Eligible if willing to discontinue. If willing to discontinue, the following washout period should be adhered to:

<u>Washout prior to screening visit</u>:

2-weeks for vitamins, probiotics, fermented drinks (e.g. kefir, kombucha)
2-weeks for omega 3 supplements ≤2 g/day
4-weeks for omega 3 supplements >2g/day

<u>Washout prior to baseline visit:</u>

4-weeks for probiotics, fermented drinks, vitamins, and omega-3 supplements ≤2g/day
6 weeks for omega-3 supplements >2g/day

- History of liver, kidney, or autoimmune disease
- Prior cardiovascular event (e.g., stroke, heart attack)
- Current pregnancy or intention of pregnancy within the next 12 months
- Lactation within the prior 6 months
- Pecan allergy/intolerance/sensitivity/dislike

- Antibiotic use within the prior four weeks
- Oral steroid use within the prior four weeks
- Use of tobacco or nicotine-containing products within the past 6 months
- History of cancer at any site within the past 10 years (eligible if ≥10 years without recurrence) or non-melanoma skin cancer within the past 5 years (eligible if ≥5 years without recurrence)
- Participation in another clinical trial within 60 days of baseline
- Currently following a restricted or weight-loss diet
- Prior bariatric surgery
- Intake of >14 alcoholic drinks/week and/or not willing to avoid alcohol consumption for 48 hours prior to test visits
- Principal Investigator discretion related to the potential participant's ability to adhere to the study requirements, including being able to come to attend visits
- Does not speak and/or understand English
- Unwilling to refrain from donating blood and/or plasma during the study
- Weight <110 lb
- Unwilling/unable to eat 1.5 oz of pecans every day as a snack during the duration of the study
- Routine use of OTC medications that affect the outcomes of interest
- Unwilling to refrain from starting to take any supplements, vitamins, nutritional products, or health foods that are not prescribed by a doctor for the duration of the study
- Unwilling to contact study staff before enrolling in other health-related research and avoid participating in any research that may interfere with this study
- For individuals taking thyroid medication: abnormal thyroid stimulated hormone (TSH) concentration, or change in dose of thyroid medication within the last 6 months

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

Insert subject withdrawal criteria (e.g., safety reasons, failure of subject to adhere to protocol requirements, subject consent withdrawal, disease progression, etc.).

Participants will be withdrawn from the study for the following reasons:

- Risks to the other participants/research team members, disruptive behavior during the study visit, or food pick-ups
- Diagnosis of a disease listed as an exclusion criterion or a serious medical condition requiring active intervention (assessed by review of medical history form or participant report)
- Prescription of anti-hypertensive, lipid-lowering, or glucose-lowering drugs (assessed by review of medical history form or participant report)
- Prescription of steroids or antibiotics for longer than 1 week
- Pregnancy

3.3.2 Follow-up for withdrawn subjects

Describe when and how to withdraw subjects from the study; the type and timing of the data to be collected for withdrawal of subjects; the follow-up for subjects withdrawn from investigational treatment.

No safety concerns; no reason for follow-up. Data from individuals who withdraw from the study will be used in an intent-to-treat analysis.

4.0 Recruitment Methods

- Upload recruitment materials for your study in CATS IRB (http://irb.psu.edu). **DO NOT** include the actual recruitment wording in this protocol.
- StudyFinder: If StudyFinder (http://studyfinder.psu.edu) is to be used for recruitment purposes, separate recruitment documents do not need to be uploaded in CATS IRB. The necessary information will be captured from the StudyFinder page in your CATS IRB study.
- Any eligibility screening questions (verbal/phone scripts, email, etc.) used when contacting potential participants must be uploaded to your study in CATS IRB (http://irb.psu.edu).

[Do not type here]

4.1 Identification of subjects

Describe the source of subjects and the methods that will be used to identify potential subjects (e.g., organizational listservs, established recruitment databases, subject pools, medical or school records, interactions during a clinic visit, etc.). If not recruiting subjects directly (e.g., database query for eligible records or samples) state what will be queried, how and by whom.

StudyFinder:

- If you intend to use StudyFinder (http://studyfinder.psu.edu) for recruitment purposes, include this method in this section.
- Information provided in this protocol, including the description of study procedures, compensation, and recruitment, needs to be consistent with information provided on the StudyFinder page in your CATS IRB study.

For research utilizing **Penn State Health patient data**, please note the following:

- Submissions using **Enterprise Information Management (EIM)** for recruitment, and for non-Hershey locations as applicable, attach your EIM Design Specification form in CATS IRB (http://irb.psu.edu). See "HRP-103- Investigator Manual, Study Recruitment" for additional information.
- Direct contact with patients for research recruitment that does not occur in person will require review of the contact list by Penn State Health's Printer Services, see links below. It is the study team's responsibility to assure removal of decedents from the provided data.
- Use of Printer Services Instructions https://psh.myprintdesk.net/DSF/SmartStore.aspx#!/SearchResults/810-009/false/0
- Uploading Files into Printer Services https://psh.myprintdesk.net/DSF/SmartStore.aspx#!/SearchResults/Mailing%2520list%2520Scanning/false/0.

Flyers/posters will be placed in campus buildings and facilities as well as the surrounding area (gyms, churches, supermarkets, coffee shops, offices of health care providers etc.) to identify potential participants residing in and around the State College area. Ads will also be placed in the local papers, magazines (e.g., Centre Daily Times), and coupon mailers (e.g., Valpak), which are distributed to residential homes. In addition, radio ads will be run. Websites (e.g., http://clinicaltrials.gov/, Facebook, Craig's List, StudyFinder, Viva Engage, and our lab's PSU webpage) and PSU listservs will be used to advertise the study. We will also contact individuals who have participated in previous studies and indicated to our research group that they are interested in participating in future studies. Interested

individuals will receive an email with additional study information and a link to the pre-screen survey (see attachments (Canned email to interested individuals; Pre-screening survey).

4.2 Recruitment process

Describe how potential subjects first learn about this research opportunity or indicate 'not applicable' if subjects will not be prospectively recruited to participate in the research.
Subject recruitment can involve various methods (e.g., approaching potential subjects in person, contacting potential subjects via email, letters, telephone, ResearchMatch, or advertising to a general public via flyers, websites, StudyFinder, newspaper, television, and radio).

If applicable, state whether the study team will access medical records before or after engaging the potential subject.

DO NOT include the actual recruitment material or wording in this protocol.

[Do not type here]

4.2.1 How potential subjects will be recruited.

- Public advertisements (flyers/posters/ newspaper ads/circulars/ websites and social media/ radio/listservs) in the local community (State College/ University Park area) (see attachment Recruitment Advertisements)
- Recruitment flyers (see attachment Flyers) will have a QR code that can be scanned by interested participants and will direct them to the online pre-screening survey via REDCap (see attachment Pre-Screening Survey).
- Email will be used to contact individuals who have participated in previous studies and have indicated to our research group that they are interested in participating in future studies (See attachment Email for Contacting Previous Subjects).

4.2.2 Where potential subjects will be recruited.

University Park and State College, PA and surrounding areas.

4.2.3 When potential subjects will be recruited.

Recruitment will commence once the protocol is approved and will continue until the target sample size is enrolled.

4.2.4 Screening and determining eligibility

Screening involves assessing whether or not a potential subject is eligible for a study based on the inclusion and exclusion criteria. This process only involves assessing eligibility.

Collecting information/data/biospecimens that are not related to eligibility does not meet the definition of screening and requires prior written consent. There are some specific situations in which consent is not required prior to screening activities.

Answer the following items to describe the screening process and determine if prior consent and/or HIPAA authorization is required.

4.2.4.1 For the purpose of screening/determining eligibility, is the potential subject providing information through oral or written communication (e.g. survey or verbally responding to answers)?

☒ Yes [NOTE: HIPAA authorization or a waiver of HIPAA authorization may be necessary – see section 6.0]

Participants will complete a REDCap pre-screening survey (see attachment Pre-Screening Survey) and a telephone screening (see attachment Telephone Screening Form) to assess eligibility. Participants will also be asked to complete a medical history form (see attachment Medical History Form). The information will be recorded and stored by the research team.

Pre-screening survey

Individuals that respond to study advertisements will be directed via an email from our lab's account (dchlab@psu.edu) (see attachment Canned Email to Interested Individuals) to complete the online pre-screening survey via REDCap (See attachment Pre-Screening Survey). Individuals that call the lab after they see a study advertisement will be briefly informed about the study, and their name and e-mail address will be requested (see attachment Verbal Script_TelephoneCall) so that they can be directed via our lab email to complete the online pre-screening survey via REDCap. Individuals that complete the pre-screening online survey and are eligible based on the included questions, will be phone screened for eligibility.

Telephone screening

Individuals who are eligible based on the online pre-screening survey will be contacted via our lab's email (dchlab@psu.edu) (see attachment Canned Email to Individuals Eligible for Telephone Screening) to obtain consent for the telephone screening. The consent for research screening procedures form will be administered via REDCap (see attachment HRP-585 Screening Consent Form). Via REDCap, individuals will be prompted to read through the Screening Consent Form after which they will be asked to indicate whether or not they consent to being called for a telephone screening. If an individual agrees to provide consent, they will be prompted to schedule their telephone screening with Calendly, an online appointment scheduling tool (https://calendly.com/ket5502-psu/30min).

A member of the research team will call individuals that consent to a telephone screening call using the contact information provided in the pre-screening survey. The telephone screening interview will be conducted according to the Telephone Screening Form (see attachment Telephone Screening Form). Research staff will either use a paper form or enter data directly into REDCap. Based on the answers to the questions, participants deemed eligible will be scheduled for a clinic screening visit. Participants eligible for the screening visit will receive a confirmation email with the visit instructions at the time the visit is scheduled (see attachment Clinic Screening Appointment Confirmation Email), and attached to the email will be the written informed consent form (see attachment HRP-580 Written Consent Form). Participants will also be asked to complete a medical history form via REDCap within 3 days of their screening appointment (see attachment Medical History Form), and a reminder will be sent via our lab's email (dchlab@psu.edu) every 24 hours until completion (up to 3 total reminders). If participants do not complete the medical history form

prior to the screening visit, it will be completed at the screening visit via REDCap or using a paper form.

☐ No

4.2.4.2 Is eligibility being determined by obtaining identifiable private information or biospecimens by accessing records or stored identifiable biospecimens?

☐ Yes [NOTE: HIPAA authorization or a waiver of HIPAA authorization may be necessary – see section 6.0]

[Describe what is being accessed here. Indicate if the information will be recorded or stored by the research team.]

☒ No

4.2.4.3 Is the potential subject being asked to do any activity for screening and eligibility purposes beyond what is described above (e.g. fast, blood test)?

☒ Yes [NOTE: consent process or waiver of consent is required – see section 5.0]

Participants will be asked to fast for 12 hours, avoid over-the-counter medications and alcohol for 48 hours prior to the clinic screening appointment.

☐ No

4.2.4.4 Is the screening data to be used for purposes other than eligibility or recruitment (e.g. retained for data analysis or for other purposes)?

☒ Yes [NOTE: consent process or waiver of consent is required – see section 5.0]

The screening data will be retained for data analysis, e.g. describing the characteristics of screeners vs. participants that were randomized, completed etc.

☐ No

5.0 Consent Process and Documentation

Refer to the following materials:

- The “HRP-090- SOP - Informed Consent Process for Research” outlines the process for obtaining informed consent.
- The “HRP-091– SOP - Written Documentation of Consent” describes how the consent process will be documented.
- The “HRP-314- Worksheet - Criteria for Approval” section 7 lists the required elements of consent.
- The “HRP-312- Worksheet - Exemption Determination” includes information on requirements for the consent process for exempt research. In addition, the CATS IRB Library contains consent guidance and templates for exempt research.
- The CATS IRB library contains various consent templates for expedited or full review research that are designed to include the required information.

- Add the consent document(s) to your study in CATS IRB (http://irb.psu.edu). Links to Penn State's consent templates are available in the same location where they are uploaded. **DO NOT** include the actual consent wording in this protocol.

[Do not type here]

5.1 Consent Process:

Check all applicable boxes below (at least one of the first four boxes must be checked):

☒ **Written documentation of consent: Informed consent will be sought and documented with a written consent form** *[Complete Sections 5.2 and 5.6; If this is the only box checked, mark Sections 5.3, 5.4 and 5.5 as 'Not applicable']*

☒ **Waiver of documentation of consent: Informed consent will be sought but subject signature is not required (e.g. implied or verbal consent will be obtained)** *[Complete Sections 5.2, 5.3 and 5.6; If this is the only box checked, mark Sections 5.4 and 5.5 as 'Not applicable']*

☐ **Alteration of consent process: Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception).** *[Complete section 5.2, 5.4 and 5.6; If this is the only box checked, mark Section 5.5 as 'Not applicable']*

☐ **Waiver of consent: Informed consent will not be obtained** *[Complete Section 5.5; If this is the only box checked, mark Sections 5.2, 5.3, 5.4 and 5.6 as 'Not applicable']*

If you believe that the research activities outlined meet one or more of the criteria outlined in "HRP-312- Worksheet- Exemption Determination", check the following box in addition to a consent checkbox above.

☐ **Exempt Research - By checking this box, you are verifying that the consent process will disclose the following:**

- **For all research**: Penn State affiliation; name and contact information for the researcher and advisor (if the researcher is a student); the activities involve research; the procedures to be performed; participation is voluntary; that there are adequate provisions to maintain the privacy interests of subjects and the confidentiality of the data; permission for use of data can be withdrawn for research activities involving the collection and use of identifiable data.

- **For research that uses student educational records:** the records that may be used; the purpose of using those records; the party or class of parties to whom the records may be shared; and that if an adult student (or a parent of a student who is not an adult) requests, the school will provide them with a copy of the records shared. Additionally, the parent or adult student will *sign and date* the consent.

Note: If this box has been checked, mark Sections 5.3, 5.4, 5.5, and 5.6 as "Not applicable." If the investigator's assessment is inaccurate, an IRB Analyst will request revision to the protocol and ask that consent forms and recruitment materials be submitted. Except for exemptions where Limited IRB Review is required (see "HRP-312- Worksheet- Exemption Determination") or where otherwise requested by the IRB, consent forms and recruitment materials are generally not reviewed nor approved by the PSU HRPP for research undergoing exempt review.

5.2 Obtaining Informed Consent

5.2.1 Consent Process

Describe the consent process (when, where, and how), including how subjects are provided the consent language and how subjects indicate consent. Describe the HIPAA authorization process (if applicable), making sure to state if authorization occurs during the consent process or describe a standalone authorization process.

If there are multiple consent processes, describe each process separately.

Consent for screening procedures will be obtained prior to the telephone screening call via REDCap (see attachments canned email to individuals eligible for a telephone screening; HRP-585 Screening Consent Form). The research team member conducting the telephone screening will be in a private room.

Written informed consent will be obtained at the first clinic appointment (screening visit) before any data collection procedures are conducted. The consent process will be conducted at the Clinical Research Center, Noll Laboratory in a private room. Written informed consent (see attachment HRP-580 Written Consent Form) will be obtained through physical signature on the paper form and/or through e-signatures via the CTSI-developed REDCap e-consent. E-Consent will be obtained using REDCap econsent, the REDCap project was created using the CTSI REDCap eConsent Guidance Version 02/28/2025.

5.2.2 Coercion or Undue Influence during Consent

Describe the steps that will be taken to minimize the possibility of coercion or undue influence in the consent process.

Study staff, coordinators, and investigators who are fully trained in the recruiting process will respond to potential participants during recruitment so as to avoid any coercion or undue influence.

Participation is voluntary and participants can withdraw at any time. Participants will be emailed a copy of the written consent form, at the time their screening visit is scheduled, and will be asked to read it prior to their visit. At the screening visit, a study coordinator will ask the participant if they had a chance to read the consent form prior to the visit. If not, they will be given time to read the written consent form. A study coordinator will then go through the written consent form with the participant, allowing time for the participant to ask questions throughout. Once the participant indicates they are ready, they will be asked to sign the consent form.

5.3 Waiver of Written Documentation of Consent

Review “HRP – 411 – Checklist – Waiver of Written Documentation of Consent.”

5.3.1 Indicate which of the following conditions applies to this research:

☒ The research presents no more that minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

OR

☐ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. (*Note: This condition is not applicable for FDA-regulated research. If this category is chosen, include copies of a consent form and /or parental permission form for participants who want written documentation linking them to the research.)*

OR

☐ If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. (*Note: This condition is not applicable for FDA-regulated research.)*

For distinct cultural groups, describe the alternative mechanism for documenting that informed consent was obtained:
Not applicable

5.3.2 Indicate what materials, if any, will be used to inform potential subjects about the research (e.g., a letter accompanying a questionnaire, verbal script, or implied consent form)

The Attachment HRP 585 Screening Consent will be administered via REDCap to obtain consent prior to the telephone screening.

5.4 Alteration of consent: Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception).

Review "HRP-410-Checklist -Waiver or Alteration of Consent Process" to ensure that you have provided sufficient information.

5.4.1 Indicate the elements of informed consent to be omitted or altered

Not applicable

5.4.2 Indicate why the research could not practicably be carried out without the omission or alteration of consent elements

Not applicable

5.4.3 Describe why the research involves no more than minimal risk to subjects.

Not applicable

5.4.4 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable

5.4.5 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable

5.4.6 Debriefing: Explain whether and how subjects will be debriefed after participation in the study. If subjects will not be debriefed, provide a justification for not doing so. Add any debriefing materials to the study in CATS IRB.

Not applicable

5.5 Waiver of consent: Informed consent will not be obtained

Review "HRP-410-Checklist -Waiver or Alteration of Consent Process" to ensure that you have provided sufficient information.

5.5.1 Indicate why the research could not practicably be carried out without the waiver of consent

Not applicable

5.5.2 Describe why the research involves no more than minimal risk to subjects.

Not applicable

5.5.3 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable

5.5.4 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable

5.5.5 Additional pertinent information after participation

Explain if subjects will be provided with additional pertinent information after participation.

Not applicable

5.6 Consent – Other Considerations

5.6.1 Non-English-Speaking Subjects

Indicate what language(s) other than English are understood by prospective subjects or representatives.

If subjects who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those subjects will be in that language. Indicate the language that will be used by those obtaining consent.

Indicate whether the consent process will be documented in writing with the long form of the consent documentation or with the short form of the consent documentation. Review "HRP-091 –SOP- Written Documentation of Consent" and "HRP-103 -Investigator Manual" to ensure that you have provided sufficient information.

Prospective subjects who do not understand English will not be enrolled. We do not have resources allocated to the enrollment of non-English speaking subject (e.g., translation of study materials to other languages).

5.6.2 Adults with Impaired Decision-Making Capacity

Refer to "HRP-417 -CHECKLIST- Adults with Impaired Decision-Making Capacity" for information about research involving adults with impaired decision-making capacity.

5.6.2.1 Capability of Providing Consent

Describe the process to determine whether an individual is capable of consent.

Not applicable

5.6.2.2 Adults Unable to Consent

Describe whether and how informed consent will be obtained from the legally authorized representative. Describe who will be allowed to provide informed consent. Describe the process used to determine these individual's authority to consent to research.

For research conducted in the state of Pennsylvania, review "HRP-013 -SOP- Legally Authorized Representatives, Children and Guardians" to be aware of which individuals in the state of Pennsylvania meet the definition of "legally authorized representative."

For research conducted outside of the state of Pennsylvania, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "HRP-013 - SOP- Legally Authorized Representatives, Children, and Guardians."

Not applicable

5.6.2.3 Assent of Adults Unable to Consent

Describe the process for assent of the subjects. Indicate whether assent will be required of all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not.

If assent will not be obtained from some or all subjects, provide an explanation of why not.

Describe whether assent of the subjects will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require subjects to sign assent documents.

Not applicable

5.6.3.1 Parental Permission

Describe whether and how parental permission will be obtained. If permission will be obtained from individuals other than parents, describe who will be allowed to provide permission. Describe the process used to determine these individual's authority to consent to each child's general medical care.

For research conducted in the state of Pennsylvania, review "HRP-013-SOP- Legally Authorized Representatives, Children and Guardians" to be aware of which individuals in the state of Pennsylvania meet the definition of "children."

For research conducted outside of the state of Pennsylvania, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along with the definition of "children" in "HRP-013-SOP- Legally Authorized Representatives, Children, and Guardians."

Not applicable

5.6.3.2 Assent of subjects who are not yet adults

Indicate whether assent will be obtained from all, some, or none of the children. If assent will be obtained from some children, indicate which children will be required to assent. When assent of children is obtained describe whether and how it will be documented.

Not applicable

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

This section is about the access, use or disclosure of Protected Health Information (PHI). PHI is individually identifiable health information (i.e., health information containing one or more 18 identifiers) that is transmitted or maintained in any form or medium by a Covered Entity or its Business Associate. A Covered Entity is a health plan, a health care clearinghouse or health care provider who transmits health information in electronic form. See "HRP-103 -Investigator Manual" for a list of the 18 identifiers.

[Do not type here]

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☒ **Not applicable, no identifiable protected health information (PHI) is accessed, used, or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☐ **Signed authorization will be obtained and documented.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☐ **Partial waiver for recruitment purposes only (e.g. if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Alteration to waive requirement for written documentation of authorization (e.g. verbal or implied authorization).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

This section is about the disclosure of PHI as it relates to the requested authorization waiver and/or alteration. Complete each item in this section in relation to each requested waiver of authorization and/or alteration (the last three boxes in Item #6.1). For example, if requesting a partial waiver for recruitment, these items need to address the PHI for recruitment rather than addressing the use of PHI for the entire study.

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Include the following statement as written – DO NOT ALTER
If the research does not involve a waiver or alteration of authorization, <u>remove</u> the statement and indicate as <u>not applicable</u>.

Not applicable

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Describe the plan to destroy the identifiers (associated with the waiver and/or alteration of authorization) at the earliest opportunity consistent with the conduct of the research. Include when and how identifiers will be destroyed.

If identifiers are to be retained, provide the legal, health or research justification for retaining the identifiers.

Not applicable

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

Provide reasons why the research or the portion of the research could not be conducted **without access to and use of PHI** (for which the study team is requesting the waiver and/or related to the alteration of authorization).

Not applicable

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

Provide reasons why the research or the portion of the research could not be conducted **without a signed authorization from the subjects**. If more than one waiver and/or alteration of authorization (e.g. waiver for recruitment and alteration for verbal authorization) is requested, make sure to provide reasoning for each request.

Not applicable

6.3 Waiver or alteration of authorization statements of agreement

By submitting this study for review with a waiver of authorization, you agree to the following statement – DO NOT ALTER.
If the research does not involve a waiver or alteration of authorization, remove the statement and indicate as not applicable.

Not applicable

7.0 Study Design and Procedures

Data collection materials that will be seen or used by subjects in your study must be uploaded to CATS IRB (http://irb.psu.edu). **DO NOT** include any actual data collection materials in this protocol (e.g., actual survey or interview questions).

[Do not type here]

7.1 Study Design

Describe and explain the study design.

This is a two-arm randomized parallel study. Participants will be randomized to one of the following attention and resource matched conditions for 16 weeks ± 7 days: 1) education to consume 1.5 oz./day of pecans in place of the snacks they usually eat that are higher in saturated fat and/or added sugars; 2) continue consuming their current diet with provision gift cards worth $15 monthly (equivalent value to the pecans) and matched contact with study personnel.

Assessment of outcomes will occur at baseline and the end of the intervention period (week 16 ± 7 days). At the baseline and 16 weeks, two blood samples will be collected (separated by approximately 24 hours) for endpoint analysis. Weight will be measured on both days at each time point. Central and peripheral blood pressure and pulse wave velocity will be measured on one day at each time point. Dietary intake will be assessed prior to baseline and during week 16 using 24-hour recalls. Participants will also provide a fecal collection at baseline and 16 weeks. Participants will also wear a continuous glucose monitor for 7 days prior to the first study visit and for 7 days during their last week of the study (week 16 ± 7 days).

7.2 Study Procedures

Provide a step-by-step description of all research procedures being conducted (broken down by visit, if applicable) including such information as below (where and when applicable); describe the following:

- HOW: (e.g., data collection via interviews, focus groups, forms such as surveys and questionnaires, medical/school records, audio/video/digital recordings, photographs, EKG procedures, MRI, mobile devices such as electronic tablets/cell phones, observations, collection of specimens, experimental drug/device testing, manipulation of behavior/use of deception, computer games, etc.) For surveys, indicate if subjects are able to skip questions that they don't want to answer.

- WHERE: (e.g., classrooms, labs, internet/online, places of business, medical settings, public spaces, etc.)

7.2.1 Visit 1 – Screening

Provide a description of what procedures will be performed on visit 1 or day 1 or pre-test in order of how these will be done. If your study only involves one session or visit, use this section only and delete 7.2.2.

The clinic screening appointment will be held at the Penn State Clinical Research Center (CRC). Participants will fast for 12 hours prior to the visit and avoid over-the-counter medications and alcohol for 48 hours. Participants will receive a confirmation email and an email about the appointment (See attachments Clinic Screening Appointment Reminder). At the clinic screening (see attachment Screening Data Collection Form), written informed consent will be obtained before any screening activities are conducted. The consent process will take place in a private room with the door shut. Prior to the clinic screening appointment, participants will be sent a Medical History Form (see Attachment Medical History Form) to complete via REDCap. If they do not complete it prior to the screening visit, it will be completed at the screening visit via REDCap or using a paper form.

The study coordinator will then measure body weight to the nearest 100 g with a calibrated electronic scale while the participant is wearing light clothing without shoes. Height will be measured using a stadiometer to the nearest 0.5 cm. Blood pressure will be measured with an automated machine. The measurement will be performed in the seated position after a 5-minute rest period using an appropriately sized cuff placed on the left arm (unless there is a reason that prevents this, e.g., participant reports pain or discomfort in the left arm and requests the right arm be used). Three measurements will be taken with a one-minute break between each measurement while no staff are in the room. An average of the last two measurements will be used for screening blood pressure. Females of childbearing potential will provide a urine sample for pregnancy testing. If, after these measurements it is determined that the participant is still eligible, a CRC nurse will take the blood draw (approximately 12.5 mL of blood or ~1 tablespoons will be taken). Blood samples will be sent to Quest Diagnostics to perform the following blood tests: complete blood count (CBC), comprehensive metabolic panel, iron, phosphate, lipid panel, uric acid, and HbA1c. If the initial blood draw is unsuccessful, it may need to be repeated, with permission from the participant. In addition, if a potential participant takes thyroid medicine, they must provide a current (within 6 months) lab test. If they do not have one, an extra 3.5 mL (0.2 tbsp) of blood will be taken to conduct a thyroid test. No blood taken at this visit will be stored for future use.

Participants will be contacted within one week 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 the person's eligibility. There will be no charge for the screening blood work or measurements, and participants will receive the results of their screening blood work.

If all eligibility criteria are met, participants will be called to inform them and discuss their study schedule. Once the schedule is agreed upon, participants will be sent an email (see attachment Canned Email_Participant Schedule) that includes their schedule as an attachment (see attachment Participant Schedule Template). Baseline visits will typically occur within 1 month of the screening appointment. If a participant's baseline visit is not scheduled within 3 months, the screening visit must be performed again.

7.2.2 Visit 2 – CGM fitting

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

This visit will be conducted approximately 7 days prior to visit 3 at the Penn State CRC. The visit will take approximately 15 minutes and will be conducted according to Data Collection Form_Visit 2 (see attachment). Participants will not be asked to complete any pre-visit procedures (e.g., fasting). The visit will be scheduled in the morning at approximately the same time as their baseline and endpoint testing visits. Participants will receive a reminder email at least 48 hours prior to the appointment (see attachment Canned Email_Visit 2 Appointment Reminder).

Participants will be asked to review their medical history form (see attachment Medical History Form) administered via REDCap 3 days prior to the study visit to update any changes to medications and/or health status that may affect study outcomes. Study staff will review changes to medications and/or health status with the Principal Investigator. According to PI discretion upon review of the updated medical history form, participants who are eligible to continue in the study will proceed with the testing visit, but participants will be withdrawn from the study if they have been diagnosed with a disease listed as an exclusion criterion or a serious medical condition requiring active intervention and/or medications that may affect study outcomes.

At this visit, a trained research staff member or a CRC nurse will fit the participant with an Abbott FreeStyle Libre Pro continuous glucose monitor (CGM) sensor (see attachment CGM Operator's Manual) according to the manufacturer's instructions (see attachment CGM Fitting Instructions). Hair may need to be shaved from the participant's arm if present, because this affects the adhesion of the sensor. The participants will be asked to wear the CGM until they return for visit 3. The sensor measures interstitial glucose concentrations every 15 minutes during wear. The sensor does not show the glucose value, so participants will be unaware of their values. These data will be used to calculate metrics of glucose control, e.g., mean glucose, mean time in tight range (70 and 140 mg/dL), and glycemic variability assessed by the coefficient of variability.

Participants will be asked to avoid taking vitamin C supplements or supplements containing vitamin C during the time they are wearing the sensor because vitamin C affects the sensor readings. In addition, participants will be asked to avoid taking salicylic acid (found in some pain relievers such as aspirin) because this affects the sensor readings (see attachment CGM participant information sheet).

At visit 3, a staff member will remove the sensor.

During the approximately 7-day period they are wearing the sensor, participants will be asked to take 12 saliva samples at home over two days by spitting into collection containers (e.g., passive drool method). On each day, participants will be asked to take six samples. These samples will be used to assess cortisol levels (an exploratory outcome) throughout the day as a marker of physiological stress. These samples are being completed because physiological stress is known to impact heart and metabolic health and will be used to examine inter-individual variability in response to the intervention. Participants will be provided with a sample collection kit and

detailed instructions (See Saliva Collection Instructions) for sample collection at home. Participants will return their samples at visit 3.

During the approximately 7-day period they are wearing the sensor, participants will be asked to complete three 24-hour recalls to estimate their usual dietary intake. Participants will receive an email following Visit Two with instructions and log in information for completing three 24-hour dietary recalls (see attachments Canned Email_ASA24 Instructions.docx; ASA24-DietAssessmentInstructionSheet.docx). Participants who do not complete the recalls during the 7 days period will be asked to complete one recall at visit 3 and one recall at visit 4. A reminder to complete the recalls will be included in the Visit 3 appointment reminder email (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

The Automated Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool will be used to administer the 24-hour recalls. This is an online system where participants will provide information about all foods, beverages and supplements consumed during the previous day. This system generates food group and nutrient data from the 24- hour recalls. These data will be used for calculation of diet quality assessed by the Healthy Eating Index 2020, intake of added sugars and saturated fats, as well as nutrient intake.

Prior to visit 3, participants will be asked to complete surveys about their physical activity (International Physical Activity Questionnaire; see attachment IPAQ), sleep health (see attachment Pittsburgh Sleep Quality Index Survey), stress (see attachments Perceived Stress Scale Survey, Psychological Well-being Scale, Life Events Checklist), loneliness (see attachment UCLA Loneliness Scale), and depression and anxiety symptoms (see attachment PHQ-8 and GAD-7). A link to the surveys will be emailed to the participant via a secure REDCap link 3 days prior to the baseline day 1 testing visit (see attachment Canned Email_Baseline Appointment Reminder). If participants do not complete these surveys prior to baseline day 1 testing, they will be asked to complete them during the baseline testing day 1 visit. These surveys are being completed because these factors are known to impact heart and metabolic health and will be used to examine inter-individual variability in response to the intervention. The sleep health survey is designed to assess the participants' usual sleep habits. The perceived stress survey, life events checklist, psychological well-being survey, and loneliness survey are designed to assess exposure to psychological stress. The sleep health, stress, well-being, loneliness, and depression and anxiety surveys are not diagnostic instruments for any psychological distress, and therefore pose no risk to participants, and no action is needed for safety based on responses.

7.2.3 Visit 3 – Baseline Day 1 Testing

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

The visit will be conducted according to the Baseline Data Collection Form (see attachment); a paper form will be completed, or the staff member will directly enter the data into REDCap. Participants will be asked to fast for 12 hours (except drink plenty of water), avoid over-the-counter medications and alcohol for 48 hours prior to the visit, and avoid vaccinations, including the flu shot within 2 weeks of the visit. The visit will be conducted at the Penn State CRC.

The CGM sensor will be removed.

If participants have not yet completed the surveys about sleep health (see attachment Pittsburgh Sleep Quality Index_Survey), stress (see attachment Perceived Stress Scale_Survey, Psychological Well-Being Scale, Life Events Checklist), physical activity (see attachment IPAQ), loneliness (see attachment Loneliness Scale), and depression and anxiety symptoms (see attachment PHQ8 and GAD7) they will be asked to complete them during this visit via REDCap or paper form. If participants have not completed all of their 24-dietary recalls, they will be asked to complete a recall during this visit.

Body weight will be measured, pulse wave analysis (PWA) will be performed to assess central and peripheral blood pressure, pulse wave velocity (PWV) will be measured, a blood draw and a hair sample will be taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to the Day 2 visit. If participants are not able to complete a fecal collection between their Day 1 and Day 2 visit, they may be provided with the kit and asked to do the collection the weekend prior to their visit. Females of childbearing potential will provide a urine sample for pregnancy testing. Saliva samples will be returned by the participant.

Pulse Wave Analysis (PWA)
To ensure accurate and reliable readings, participants will be asked to wear a light or short-sleeved top/shirt to their visit. Following a 5-minute seated rest period, brachial artery systolic and diastolic blood pressure will be measured using the left arm, unless there is a reason that prevents this (e.g., participant reports pain or discomfort in the left arm and requests the right arm be used), using an automated blood pressure cuff. The cuff will reinflate and obtain a pulse wave form. Central blood pressure and wave reflection characteristics (augmentation index) will then be derived from the pressure waveforms using a validated transfer function with a SphygmoCor System (AtCor Medical, Sydney, Australia). Three measurements will be taken with a one-minute break between each measurement. An average of the last two measurements will be used for data analysis. If brachial systolic blood pressure is inconsistent (i.e., >10 mm Hg difference), a fourth measurement will be taken, and the 2 closest measurements from measurements 2-4 will be used for analysis.

Pulse Wave Velocity (PWV)
Carotid-Femoral PWV will be measured using the SphygmoCor ECEL device (AtCor Medical, Sydney, Australia). To ensure accurate and reliable readings, participants will be requested to wear shorts or pants made of thin material (e.g., tights) to their visit. If participants forget to wear or bring this type of clothing, the study team will provide them with shorts to wear during the measurements. A blood pressure cuff will be placed on the participant's thigh. The cuff will inflate during the test to record the pulse waveform in the femoral artery. A simultaneous measurement of the carotid artery pressure waveform will be obtained by an applanation tonometry sensor manually held in place above the carotid artery. The measurement will be performed in the supine position immediately following the PWA measurement. Three measurements will be taken. If the measurements are inconsistent (i.e.,> 0.5 m/s difference), a fourth measurement will be taken. The three closest measurements will be averaged for data analysis.

Plasma/serum analysis
Approximately 45 mL (about 3 tbsp) will be collected at each visit. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1mL per aliquot) and stored at −80°C. At the end of the study (i.e. once all participants are done), frozen aliquots of serum/plasma will be shipped to a commercial laboratory (e.g. LabCorp and Quest Diagnostics) or taken to a laboratory on the Penn State campus (e.g. Biomarker Core Laboratory) for analysis

of the following: blood lipids and lipoprotein concentration, particle number and size, glucose and insulin, other markers of glycemia, heart disease risk, cholesterol metabolism, and/or inflammation. Remaining aliquots will be stored for future use.

Fecal collection

Participants will be asked to collect a stool sample (~50 g). They will be provided with a stool sample kit and detailed instructions (see attachment Fecal Collection Instructions) for the collection of a clean sample on Day 1 of testing and asked to bring in the collected sample on Day 2; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the subject. Samples will be frozen at −80°C until the completion of the study. At the end of the study, frozen fecal samples will be analyzed for gut bacteria composition (gut microbiome) by a laboratory that specializes in these analyses (laboratory TBD). Following the analysis, the remainder of the sample will be refrozen and stored for future use.

Hair sample

A hair sample of approximately 10-20 strands of hair will be collected to assess cortisol as a biomarker of hypothalamic-pituitary-adrenal (HPA) axis activity to assess chronic stress exposure. This sample is being completed because chronic stress is known to impact heart and metabolic health and will be used to examine inter-individual variability in response to the intervention. The sample will be collected from the posterior vertex of the scalp (e.g., the highest point of the back of the head). To collect the sample, a trained research staff member will use scissors to cut a small section of hair that is approximately the width of a pencil tip as close to the scalp as possible. Hair testing will be done by the Penn State Biomarker Core Lab. Participants can withdraw consent for the hair collection at any time without any effect on participation in other parts of the study.

7.2.4 Visit 4 – Baseline Day 2 Testing

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

On day 2 of baseline and endpoint visits, which occur approximately 24 hours after day 1 testing, a fasting blood sample will be collected and PWA and PWV measurements will be taken if they were not completed on Day 1 for any reason. Body weight will be taken. Fecal sample collection will be brought to the visit by the subject. If participants have not completed all of their 24-dietary recalls, they will be asked to complete a recall during this visit.

Plasma/serum analysis: A 12-hour fasting blood sample will be taken. Approximately 45 ml (about 3 Tbsp) will be collected at each visit. A typical American Red Cross blood donation is 1 pint (500 ml). Blood may be analyzed for the following: blood lipids and lipoprotein concentration, glucose and insulin, other markers of glycemia, heart disease risk, cholesterol metabolism, and/or inflammation. Remaining aliquots will be stored for future use.

Following completion of this visit. Participants will go to the Penn State Research Kitchen in 224 Henderson for randomization. Participants will be provided with a map and directions to the Research Kitchen (See attachment Research Kitchen Directions and Parking). Participants will be

informed of which study group they are in. Depending on the group, the participants will be provided with either the "Usual Diet Group Instructions" or "Pecan Group Instructions" and the information sheet will be explained. Participants in the pecan group will receive a month's supply of pre-portioned pecans. The control group will receive a $15 gift card. Each month, participants in both groups will go to the Penn State Research Kitchen for the collection of pecans or a gift card, depending on which group they are in. Participants will also receive daily adherence tracking surveys through SMS text messaging through REDCap (see attached "Daily monitoring text message pecan condition" or "Daily monitoring text message usual diet condition"). Participants can opt out of text messaging at any time. If participants opt out, they will complete a paper daily monitoring form (see attached "Paper Daily Monitoring Form Pecan condition" and "Paper Daily Monitoring Form Usual Diet Condition")

7.2.5 Visit 5 – CGM fitting week 15 ± 7 days

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

This visit will be conducted approximately 7 days prior to visit 6 at the Penn State CRC. The visit will take approximately 15 minutes and will be conducted according to Data Collection Form_Visit 5. Participants will not be asked to complete any pre-visit procedures (e.g., fasting). The visit will be scheduled in the morning at approximately the same time as their baseline and endpoint testing visits. Participants will receive a reminder email at least 48 hours prior to the appointment (see attachment Canned Email_Visit 5 Appointment Reminder).

At this visit, a trained research staff member or a CRC nurse will fit the participant with an Abbott FreeStyle Libre Pro continuous glucose monitor (CGM) sensor (see attachment CGM Operator's Manual) according to the manufacturer's instructions (see attachment CGM Fitting Instructions). Hair may need to be shaved from the participant's arm if present, because this affects the adhesion of the sensor. The participants will be asked to wear the CGM until they return for visit 3. The sensor measures interstitial glucose concentrations every 15 minutes during wear. The sensor does not show the glucose value, so participants will be unaware of their values. These data will be used to calculate metrics of glucose control, e.g., mean glucose, mean time in tight range (70 and 140 mg/dL), and glycemic variability assessed by the coefficient of variability.

Participants will be asked to avoid taking vitamin C supplements or supplements containing vitamin C during the time they are wearing the sensor because vitamin C affects the sensor readings. In addition, participants will be asked to avoid taking salicylic acid (found in some pain relievers such as aspirin) because this affects the sensor readings (see attachment CGM participant information sheet).

At visit 6, a staff member will remove the sensor.

Participants will be asked to take 12 saliva samples at home over two days by spitting into collection containers (e.g., passive drool method) during their last week in the study. On each day, participants will be asked to take six samples. These samples will be used to assess cortisol levels throughout the day as a marker of physiological stress. These samples are being completed because physiological stress is known to impact heart and metabolic health and will be used to examine inter-individual variability in response to the intervention. Participants will be provided

with a sample collection kit and detailed instructions (See Saliva Collection Instructions) for sample collection at home. Participants will return their samples at visit 6.

Participants will be asked to complete three 24-hour recalls during their last week in the study. The Automated Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool will be used to administer the 24-hour recalls. This is an online system where participants will provide information about all foods, beverages and supplements consumed during the previous day. This system generates food group and nutrient data from the 24-hour recalls. These data will be used for the calculation of diet quality assessed by the Healthy Eating Index 2020, intake of added sugars and saturated fats, as well as nutrient intake. Participants will receive an email following Visit 5 with instructions and log in information for completing three 24-hour dietary recalls (see attachments Canned Email_ASA24 Instructions.docx; ASA24-DietAssessmentInstructionSheet.docx). Participants in the pecan group will receive an additional instruction sheet for how to report pecan intake (see attachment ASA24-DietAssessmentInstructionSheet Pecan). Participants who do not complete the recalls during the 7 days period will be asked to complete one recall at visit 6 and one recall at visit 7. A reminder to complete the recalls will be included in the Visit 6 appointment reminder email (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

Participants will be asked to complete surveys about their physical activity (International Physical Activity Questionnaire; see attachment IPAQ), sleep health (see attachment Pittsburgh Sleep Quality Index Survey), stress (see attachments Perceived Stress Scale Survey, Psychological Well-being Scale, Life Events Checklist), loneliness (see attachment UCLA Loneliness Scale), and depression and anxiety symptoms (see attachment PHQ-8 and GAD-7). A link to the surveys will be emailed to the participant via a secure REDCap link 3 days prior to the baseline day 1 testing visit (see attachment Canned Email_Baseline_Endpoint Appointment Reminder). These surveys will be completed so that changes in physical activity, sleep health, and stress can be captured because these factors are known to impact heart and metabolic health. This will provide preliminary data for future investigations. If participants do not complete these surveys prior to endpoint day 1 testing, they will be asked to complete them during the endpoint testing day 1 visit.

7.2.6 Visit 6 – Endpoint Day 1 Testing

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

The visit will be conducted according to the Data Collection Form_ Endpoint Day 1 (see attachment); a paper form will be completed, or the staff member will directly enter the data into REDCap. Participants will be asked to fast for 12 hours (except drink plenty of water), avoid over-the-counter medications and alcohol for 48 hours prior to the visit, and avoid vaccinations, including the flu shot within 2 weeks of the visit. The visit will be conducted at the Penn State CRC.

If participants have not yet reviewed their Medical History Form or completed the survey about sleep health (see attachment Pittsburgh Sleep Quality Index_Survey), stress (see attachment Perceived Stress Scale_Survey, Psychological Well-Being Scale, Life Events Checklist), physical activity (see attachment IPAQ), loneliness (see attachment Loneliness Scale), and depression

and anxiety symptoms (see attachment PHQ8 and GAD7) they will be asked to complete them during this visit via REDCap or paper form. If participants have completed <3 24-dietary recalls, they will be asked to complete a recall during this visit.

The CGM will be removed. Body weight will be measured, pulse wave analysis (PWA) will be performed to assess central and peripheral blood pressure, pulse wave velocity (PWV) will be measured, and a blood draw will be taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to the Day 2 visit. If participants are not able to complete a fecal collection between their Day 1 and Day 2 visit, they may be provided with the kit and asked to do the collection the weekend prior to their visit. Females of childbearing potential will provide a urine sample for pregnancy testing. Participants will return their saliva samples.

Pulse Wave Analysis (PWA)
To ensure accurate and reliable readings, participants will be asked to wear a light or short-sleeved top/shirt to their visit. Following a 5-minute seated rest period, brachial artery systolic and diastolic blood pressure will be measured using the left arm, unless there is a reason that prevents this (e.g., participant reports pain or discomfort in the left arm and requests the right arm be used), using an automated blood pressure cuff. The cuff will reinflate and obtain a pulse wave form. Central blood pressure and wave reflection characteristics (augmentation index) will then be derived from the pressure waveforms using a validated transfer function with a SphygmoCor System (AtCor Medical, Sydney, Australia). Three measurements will be taken with a one-minute break between each measurement. An average of the last two measurements will be used for data analysis. If brachial systolic blood pressure is inconsistent (i.e., >10 mm Hg difference), a fourth measurement will be taken, and the 2 closest measurements from measurements 2-4 will be used for analysis.

Pulse Wave Velocity (PWV)
Carotid-Femoral PWV will be measured using the SphygmoCor ECEL device (AtCor Medical, Sydney, Australia). To ensure accurate and reliable readings, participants will be requested to wear shorts or pants made of thin material (e.g., tights) to their visit. If participants forget to wear or bring this type of clothing, the study team will provide them with shorts to wear during the measurements. A blood pressure cuff will be placed on the participant's thigh. The cuff will inflate during the test to record the pulse waveform in the femoral artery. A simultaneous measurement of the carotid artery pressure waveform will be obtained by an applanation tonometry sensor manually held in place above the carotid artery. The measurement will be performed in the supine position immediately following the PWA measurement. Three measurements will be taken. If the measurements are inconsistent (i.e.,> 0.5 m/s difference), a fourth measurement will be taken. The three closest measurements will be averaged for data analysis.

Plasma/serum analysis
Approximately 45 mL (about 3 tbsp) will be collected at each visit. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1mL per aliquot) and stored at −80°C. At the end of the study (i.e. once all participants are done), frozen aliquots of serum/plasma will be shipped to a commercial laboratory (e.g. LabCorp and Quest Diagnostics) or taken to a laboratory on the Penn State campus (e.g. Biomarker Core Laboratory) for analysis of the following: blood lipids and lipoprotein concentration, particle number and size, glucose and insulin, other markers of glycemia, heart disease risk, cholesterol metabolism, and/or inflammation. Remaining aliquots will be stored for future use.

Fecal collection

Participants will be asked to collect a stool sample (~50 g). They will be provided with a stool sample kit and detailed instructions (see attachment Fecal Collection Instructions) for the collection of a clean sample on Day 1 of testing and asked to bring in the collected sample on Day 2; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the subject. Samples will be frozen at −80°C until the completion of the study. At the end of the study, frozen fecal samples will be analyzed for gut bacteria composition (gut microbiome) by a laboratory that specializes in these analyses (laboratory TBD). Following the analysis, the remainder of the sample will be refrozen and stored for future use.

Hair sample

A hair sample of approximately 10-20 strands of hair will be collected to assess cortisol as a biomarker of hypothalamic-pituitary-adrenal (HPA) axis activity to assess chronic stress exposure. This sample is being completed because chronic stress is known to impact heart and metabolic health and will be used to examine inter-individual variability in response to the intervention. The sample will be collected from the posterior vertex of the scalp (e.g., the highest point of the back of the head). To collect the sample, a trained research staff member will use scissors to cut a small section of hair that is approximately the width of a pencil tip as close to the scalp as possible. Hair testing will be done by the Penn State Biomarker Core Lab. Participants can withdraw consent for the hair collection at any time without any effect on participation in other parts of the study.

7.2.7 Visit 7 – Endpoint Day 2 Testing

Provide a description of what procedures will be performed on visit 2 or day 2 or post-test in order of how these will be done. If your study involves more than two sessions or visits replicate this section for each additional session or visit (e.g., 7.2.3, 7.2.4, etc.). If your study involves only one session or visit, delete this section.

On day 2 of the endpoint visit, which occurs approximately 24 hours after day 1 testing, a fasting blood sample will be collected, and PWA and PWV measurements will be taken if they were not completed on Day 1 for any reason. Body weight will be taken. Fecal sample collection will be brought to the visit by the subject. If participants have not completed all of the required 24 hour recalls they will be asked to complete a recall during this visit.

Plasma/serum analysis: A 12-hour fasting blood sample will be taken. Approximately 45 ml (about 3 Tbsp) will be collected at each visit. A typical American Red Cross blood donation is 1 pint (500 ml). Blood may be analyzed for the following: blood lipids and lipoprotein concentration, glucose and insulin, other markers of glycemia, heart disease risk, cholesterol metabolism, and/or inflammation. Remaining aliquots will be stored for future use.

7.3 Duration of Participation

Describe how long subjects will be involved in this research study. Include the number of sessions and the duration of each session - consider the total number of minutes, hours, days, months, years, etc.

Each participant will be in the study for up to 7 months. The study is 4 months, and it may take up to 3 months before an eligible person is scheduled for their baseline visit. The screening visit will take approximately 1 hour, and the CGM fitting appointments will take approximately 15 minutes. The testing visits will take approximately 1 hour on day 1 and approximately 45 minutes on day 2. The screening visit, CGM visits, and 4 testing visits (7 visits total) will take approximately 5 hours total.

Monthly appointment for pecans/gift cards and adherence monitoring will take approximately 15 minutes (1 hour for 4 visits – 1 per month). Therefore, this study will involve approximately 6 hours.

8.0 Number of Subjects and Statistical Plan

8.1 Number of Subjects

Indicate the maximum number of subjects to be accrued/enrolled, to include all persons who sign consent for the study. If applicable, distinguish between the number of subjects who are expected to be enrolled and screened, and the number of subjects needed to complete the research procedures (i.e., numbers of subjects excluding screen failures.)

To be powered, 147 individuals need to be randomized and 128 need to complete the research procedures. To randomize this number, it is expected that 442 individuals will be enrolled and screened.

8.2 Sample Size Determination

If applicable, provide a justification of the sample size outlined in section 8.1 to include reflections on, or calculations of, the power of the study.

Sample size calculations show 128 participants (64 per group) will provide 80% power to detect a 0.08 (SD 0.16)[20] percentage point between-group difference in HbA1C (α=0.05). In total, 147 participants will be randomized to allow for an attrition rate of ~15%.

8.3 Statistical or Analytic Methods

Describe the statistical methods (or non-statistical methods of analysis) that will be employed.

All data collected from randomly assigned participants will be included in data analyses consistent with intent-to-treat principles. Assumptions for all statistical tests will be checked and confirmed prior to conducting analyses for hypothesis testing. The primary analyses for all outcomes will assess the between-group (pecan or usual diet) differences in the change from baseline using linear regression. The change from baseline will be calculated by subtracting the endpoint value from the baseline value. Secondary analyses will be conducted to assess the between-group differences in endpoint means for all outcomes using linear mixed models. This will be done to confirm the primary analyses. Group will be included as a fixed effect, and visit will be included as a repeated effect. Intervention effects will be determined by examining the group-by-visit interaction. When significant group-by-visit interaction is detected, post hoc testing will be conducted, and the Tukey-Kramer method will be used to adjust for multiple comparisons.

9.0 Data and Safety Monitoring Plan

This section is required when research involves more than Minimal Risk to subjects as defined in "HRP-001 SOP- Definitions."

Minimal Risk is defined as the probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For research involving prisoners, Minimal Risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Please complete each section below if the research involves more than minimal risk to subjects or indicate not applicable. If reviewed at a convened board, the board may require the completion of this section. Note: For cancer-related trials, PRC will ask for data safety monitoring for low-risk trials outside of the IRB process.

[Do not type here]

9.1 Periodic evaluation of data

Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Not applicable

9.2 Data that are reviewed

Describe the data that are reviewed, including safety data, untoward events, and efficacy data.

Not applicable

9.3 Method of collection of safety information

Describe the method by which the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls and with subjects).

Not applicable

9.4 Frequency of data collection

Describe the frequency of data collection, including when safety data collection starts.

Not applicable

9.5 Individuals reviewing the data

Identify the individuals who will review the data. The plan might include establishing a data and safety monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

Not applicable

9.6 Frequency of review of cumulative data

Describe the frequency or periodicity of review of cumulative data.

Not applicable

9.7 Statistical tests

Describe the statistical tests for analyzing the safety data to determine whether harms are occurring.

Not applicable

9.8 Suspension of research

Describe any conditions that trigger an immediate suspension of research.

Not applicable

10.0 Risks

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider all types of risk including physical, psychological, social, legal, and economic risks. **Note: Loss of confidentiality is a potential risk when conducting human subject research and must be listed here.**

- If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.
- If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.
- If applicable, describe risks to others who are not subjects.

Gastrointestinal symptoms:
Some participants may experience GI (stomach) upset from the changes to their diet with the incorporation of the pecans; symptoms may include, but are not limited to, any of the following: constipation/diarrhea, nausea, and bloating. This will likely subside once the participant becomes accustomed to the study food.

Food Allergies:
Individuals will be asked to report any food allergies during the telephone screening; however, it is possible that an unknown pecan allergy may manifest during the study. This is most likely to occur within the first week of the study. Each day participants will be asked to complete a daily monitoring form. In addition, we ask participants to please inform study staff immediately should any adverse events occur.

Food Preparation
Pecans will be purchased from local stores or food delivery services and pre-portioned into 1.5 oz. servings by kitchen staff according to food safety protocols. There is a possibility of foodborne illness or cross-contamination, but risks will be minimized by proper food handling, handwashing, and cleaning procedures.

Fasting:
After a 12-hour overnight fast (except drinking plenty of water), participants may feel slightly faint or dizzy. This risk will be minimized as participants will be reminded to drink water the morning of the blood draw and will be provided with a snack after all testing required for the study visit is completed.

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 medical staff draw the blood in a clinical setting using sterile supplies. If dizziness or fainting occurs, the symptoms will be alleviated by having the participant lie flat with their feet raised. The medical staff will ask that the participant remains at the clinic until their blood pressure has been checked and they are cleared from any further risk.

Pulse Wave Analysis (PWA) and Pulse Wave Velocity

There are no known risks associated with these measurements. The sensation of pressure from the blood pressure cuff or hand-held probe may be uncomfortable. 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 (occurring in less than ½ of 1% of patients) and it is typically not uncomfortable and does not require treatment.

Stool Collection
Participants may experience some level of embarrassment or discomfort from being asked to collect stool samples. However, participants will be provided with detailed instructions on how to collect the samples within the comfort of their own home, and at their convenience, to help reduce concerns.

Loss of Confidentiality
There is always a potential for loss of confidentiality despite our best efforts. To prevent this from occurring all records are coded with a unique ID number and no names are used. Records containing names or other identifying information are kept under lock at the PI's research office. All records associated with an individual's participation in the study will be subject to the usual confidentiality standards applicable to medical records. In the event of publication of this research, no personal identifying information will be disclosed.

Continuous glucose monitoring
Skin irritation or allergic reactions may occur at the sensor site. There is also a slight chance of infection, this risk will be minimized and most likely eliminated by having trained staff fit the sensor.

11.0 Potential Benefits to Subjects and Others

11.1 Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. If there is no direct benefit to subjects, indicate as such. Compensation is not considered a benefit. Compensation should be addressed in section 13.0.

Participants will receive their screening laboratory results, complete blood count (CBC), comprehensive metabolic panel, iron, phosphate, lipid panel, uric acid, and HbA1c, at no cost.

11.2 Potential Benefits to Others

Describe the potential benefits to society or others.

The results will contribute to understanding the role of snacking in cardiometabolic health. These results may inform guidelines e.g., the Dietary Guidelines for Americans that would benefit the U.S. population.

12.0 Sharing Results with Subjects

Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how information will be shared.

Screening results will be provided to all potential participants (regardless of their eligibility status) within 2 weeks of their screening appointment and will be sent to their mailing address via postal delivery. All screening results will be reviewed by the Nurse Practitioner or Physician at the Clinical Research Center. Should any abnormal lab values be identified that warrant further evaluation, the individual will be contacted (by the Study Coordinator or the CRC Nurse Practitioner, or the Physician) and asked to schedule a visit with their primary care physician.

At the completion of the study, the key findings from the study overall may be posted on our laboratory's website. Upon request, individual results may be given to participants at the completion of all study-related data collection and analyses. Study results will not be provided to participants during the study because knowledge of the results may change behavior and influence the study results.

13.0 Subject Payment and/or Travel Reimbursements

Describe the amount, type (cash, check, gift card, other), reason/purpose (travel reimbursement or compensation for their time, inconvenience, discomfort), and timing of any subject payment or travel reimbursement. If there is **no** subject payment or travel reimbursement, indicate as not applicable.

Extra or Course Credit: Describe the amount of credit **and** the available alternatives. Alternatives should be equal in time and effort to the amount of course or extra credit offered. It is not acceptable to indicate that the amount of credit is to be determined or at the discretion of the instructor of the course.

Approved Subject Pool: Indicate which approved subject pool will be used; include in response below that course credit will be given and alternatives will be offered as per the approved subject pool procedures.

Participants will be paid up to $150 as compensation for the time and burden associated with participating in the study. Payment will be made following completion of the endpoint day 2 testing. Payment will be prorated as follows for partial completion.

Participation in baseline day 1 and day 2 testing = $30
Participation in endpoint day 1 and day 2 testing = $120

14.0 Economic Burden to Subjects

14.1 Costs

Describe any costs that subjects may be responsible for because of participation in the research.

The participants will not bear any costs due to their participation in the study.

Participants are responsible for their own transportation to the Clinical Research Center for study visits and to the Penn State Research Kitchen. At the Clinical Research Center and the Metabolic Kitchen, free parking is available.

14.2 Compensation for research-related injury

If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

If there is no sponsor agreement that addresses compensation for medical care for research subjects with a research-related injury, include the following text as written - DO NOT ALTER OR DELETE:
It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Costs for the treatment of research-related injuries will be charged to subjects or their insurance carriers.

For sponsored research studies with a research agreement with the sponsor that addresses compensation for medical care for research-related injuries, include the following text as written - DO NOT ALTER OR DELETE:

It is the policy of the institution to provide neither financial compensation nor free medical treatment for research-related injury. In the event of injury resulting from this research, medical treatment is available but will be provided at the usual charge. Such charges may be paid by the study sponsor as outlined in the research agreement and explained in the consent form.

Not applicable – the research does not involve more than minimal risk.

15.0 Resources Available

15.1 Facilities and locations

Identify and describe the facilities, sites, and locations where recruitment and study procedures will be performed.

If research will be conducted outside the United States, describe site-specific regulations or customs affecting the research, and describe the process for obtaining local ethical review. Also, describe the principal investigator's experience conducting research at these locations and familiarity with local culture.

Penn State University Clinical Research Center
The clinical aspects of this study will be conducted at the Clinical Research Centre (CRC) on the University Park campus of the Pennsylvania State University. The CRC is a purpose-built research unit that supports human clinical research trials, and is fully equipped with exam rooms, invasive and general procedure rooms and five hospital-style bedrooms with bathrooms. There is also a specimen processing room with refrigerated and unrefrigerated centrifuges for the preparation of samples. The study investigators will work closely with experienced CRC staff (physicians, nurse practitioners, registered nurses, and research technologists) to optimize and facilitate the research protocol. The principal investigators and project coordinators are experienced with conducting research at this location and have conducted multiple clinical trials at this location previously.

The Penn State Research Kitchen
This is a state-of-the-art facility consisting of a fully-equipped kitchen specifically designed for nutrition studies. In addition, this area is available for small group meetings with study participants and counseling/information exchange with small groups of individuals.

15.2 Feasibility of recruiting the required number of subjects

Indicate the number of potential subjects to which the study team has access. Indicate the percentage of those potential subjects needed for recruitment.

We have previously done studies of this nature and have not had difficulty recruiting. We use several different recruitment methods and have budgeted sufficient resources for advertising. Additionally, we have access to a large database of previous participants who have consented to further contact.

15.3 PI Time devoted to conducting the research

Describe how the PI will ensure that a sufficient amount of time will be devoted to conducting and completing the research. Consider outside responsibilities as well as other ongoing research for which the PI is responsible. Please only provide a response for the principal investigator – do **not** include information about any other study team members.

The Principal Investigator will be responsible for assuring through personal contact with the research and clinical staff and coordinators that each individual clearly understands and accepts the obligations incurred in the undertaking of this clinical trial.

The Principal Investigator will ensure that the research staff fully understand the nature of the protocol and the requirements for an adequate and well-controlled study; the obligation to conduct the clinical investigation in accordance with the applicable federal regulations; the obligation to obtain informed consent; the obligation to obtain IRB review and approval of a clinical investigation before the investigation may be initiated and to ensure continuing review of the study by the IRB.

15.4 Availability of medical or psychological resources

Describe the availability of medical or psychological resources that subjects might need as a result of their participation in the study.

Nursing staff are always present during clinical testing. Highly trained nursing staff will perform procedures requiring licensure or demonstrated competency e.g., blood pressure, blood draws. A physician or CRNP will review all screening visit results as part of the eligibility assessment of a participant. Should an individual require psychological services they will be referred to the on-campus clinic: Psychological Clinic, 314 Moore Bldg., University Park, Phone: 865-2191.

15.5 Process for informing Study Team

Describe the training plans to ensure members of the research team are informed about the protocol and their duties.

All study staff will be required to complete the Human Participant Training and Bloodborne Pathogen Training as mandated by the Pennsylvania State University Office of Research Protections. In addition, as part of the initial training for this study, all staff members (e.g., project managers, research coordinators, assistants, and Clinical Research Center [CRC] nursing staff) will conduct an initial project start-up meeting to review the scientific protocol and ensure all study procedures are in place.

16.0 Other Approvals

16.1 Other Approvals from External Entities

Describe any approvals that will be obtained prior to commencing the research (e.g., from engaged cooperating institutions IRBs who are also reviewing the research and other required review committees, community leaders, schools, research locations where research is to be conducted by the Penn State investigator, funding agencies, etc.).

IBC approval will be obtained for the collection and analysis of blood and fecal samples.

16.2 Internal PSU Ancillary Reviews

DO NOT ALTER OR DELETE:
Ancillary reviews are reviewed by other compliance groups or individuals within Penn State that inform the IRB's review of a new study or a modification to an existing study.

PSU IRB may set applicable ancillary reviews for your study. Please refer to the "HRP-309 Worksheet – Ancillary Review Matrix" for more information (found in the CATS Library).

[Do not type here]

17.0 Multi-Site Study

If this is a multi-site study (i.e., a study in which two or more institutions coordinate, with each institution completing all research activities outlined in a specific protocol) and **the Penn State PI is the lead investigator**, describe the processes to ensure communication among sites in the sections below.

[Do not type here]

17.1 Other sites

List the name and location of all other participating sites. Provide the name, qualifications and contact information for the principal investigator at each site and indicate which IRB will be reviewing the study at each site.

Not applicable

17.2 Communication Plans

Describe the plan for regular communication between the overall study director and the other sites to ensure that all sites have the most current version of the protocol, consent document, etc. Describe the process to ensure all modifications have been communicated to sites. Describe the process to ensure that all required approvals have been obtained at each site (including approval by the site's IRB of record). Describe the process for communication of problems with the research, interim results, and closure of the study.

Not applicable

17.3 Data Submission and Security Plan

Describe the process and schedule for data submission and provide the data security plan for data collected from other sites. Describe the process to ensure all engaged participating sites will safeguard data as required by local information security policies.

Not applicable

17.4 Subject Enrollment

Describe the procedures for coordination of subject enrollment and randomization for the overall project.

Not applicable

17.5 Reporting of Adverse Events and New Information

Describe how adverse events and other information will be reported from the clinical sites to the overall study director. Provide the timeframe for this reporting.

Not applicable

17.6 Audit and Monitoring Plans

Describe the process to ensure all local site investigators conduct the study appropriately. Describe any on-site auditing and monitoring plans for the study.

Not applicable

18.0 Adverse Event Reporting

18.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.0 Study Monitoring, Auditing, and Inspecting

19.1 Auditing and Inspecting

By submitting this study for review, you agree to the following statement – DO NOT ALTER OR DELETE:

The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

20.0 References

List relevant references in the literature which highlight methods, controversies, and study outcomes.

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4. Evert AB, Dennison M, Gardner CD, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. *Diabetes Care*. 2019;42(5):731.
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21.0 Confidentiality, Privacy and Data Management

For data level classification: https://security.psu.edu/awareness/icdt/

For approved UP/Commonwealth storage platforms:
https://security.psu.edu/awareness/storage/
https://datastoragefinder.psu.edu/computing/backup-storage/finder

Please visit https://datastoragefinder.psu.edu and https://security.psu.edu/awareness/storage/ for assistance with identifying appropriate data storage options. If the software to be used does not appear on that site, please visit https://procurement.psu.edu/electronic-click-through-contracts to consider whether a software request form must be completed.

NOTE: Please refer to PSU Policy AD95 for information regarding information classification and security standards and requirements. **UP/Commonwealth campuses:** If you have questions about Penn State's Policy AD95 or standards or need a consultation regarding data security, please contact Penn State IT – Information Security at security@psu.edu. **College of Medicine:** If you have questions about Penn State's Policy AD95 or standards or need a consultation regarding data security, please contact Philemon Canakis in the Penn State IT Security Group at pcanakis@pennstatehealth.psu.edu.

21.1 Which of the following identifiers will be recorded for the research project? Check all that apply. If none of the following identifiers will be recorded, do not check any of the boxes.

	Hard Copy Data	Electronic Stored Data
Names and/or initials (including on signed consent documents)	☒	☒
All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes,	☒	☒
All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older	☒	☒
Telephone numbers	☒	☒
Fax numbers	☐	☐
Electronic mail addresses	☒	☒
Social security numbers	☐	☐
Medical record numbers	☐	☐
Health plan beneficiary numbers	☐	☐
Account numbers	☐	☐
Certificate/license numbers	☐	☐
Vehicle identifiers and serial numbers, including license plate numbers	☐	☐
Device identifiers and serial numbers	☐	☐
Web Universal Resource Locators (URLs)	☐	☐
Internet Protocol (IP) address numbers	☐	☒
Biometric identifiers, including finger and voice prints	☐	☐
Full face photographic images and any comparable images	☐	☐
Any other unique identifying number, characteristic, or code (such as the pathology number)	☐	☐
Study code number with linking list	☐	☒
Genomic sequence data	☐	☐
State ID numbers	☐	☐
Passport numbers	☐	☐
Driver's license numbers	☐	☐

21.2 Are the identifiers above linked (directly or indirectly via code list) to research data?

☐ No – skip to 21.3
☒ Yes – complete 21.2.1

21.2.1 Explain how the list that links the code to identifiers is stored, whether and how it is stored separately from coded data, and who has access:

When appropriate, a list/key that links indirect identifiers (code numbers, participant IDs, etc.) to direct identifiers should not be comingled (i.e., stored in the same location) as the identifiable data, including copies of signed informed consent forms. For some types of research, this may not be practical. In all cases, access to that list/key must be restricted to authorized project personnel.

A master list containing a study ID number and the participant's identity will be used. This file will be stored electronically in REDCap during the study and downloaded upon study completion in a secure PSU-approved location, e.g., OneDrive or SharePoint, where only approved study personnel will be able to access it through their PSU account. No study data containing study ID#'s (code numbers) will be stored with the master list. Upon completion of data collection, only the investigators and the study coordinator will have access to the list. This list will be deleted approximately 3 years after the results from all pre-specified primary and secondary outcomes are published.

21.3 Are paper records of research data (including copies of signed consent forms) being collected or stored:

☐ No – skip to 21.4
☒ Yes – complete 21.3.1 and 21.3.2

21.3.1 Where will the paper records be securely stored?

Consent forms and paper data collection sheets will be stored in a locked filing cabinet in a locked office (Chandlee Laboratory) and in the Clinical Research Centre, Noll Laboratory.

21.3.2 Will everyone on the study team have access to the stored paper records?

☐ Yes – skip to 21.4
☒ No – Explain what limitations are in place:

Only authorized project personnel will have key access to the locked filing cabinets.

21.4 Are electronic records of research data being collected or stored?

☐ No – skip to 21.5
☒ Yes – Complete rest of 21.4

Use of one of the IT-approved solutions listed is strongly recommended. If "Other" is chosen for storage of identifiable data, the IRB may set an ancillary review for further assessment of compliance with institutional data security policy.

21.4.1 How is the data being collected? (e.g., data capture using online surveys/questionnaire, surveys via email, observation of chat rooms or blogs, survey platform, application, or device)

Research staff will use PSU-owned electronic tablets for electronic data capture using REDCap (a secure electronic database provided by Penn State). Research staff and/or research participants will enter screening information (first name, last name, email address, phone number, mailing address, date of birth). Participants completing surveys at home will use their own device. Participants who complete surveys at the CRC will use a PSU-owned electronic tablet.

Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool is being used to collect dietary data.

Abbott Freestyle Libre Pro System is being used for continuous glucose monitoring for 7 days at the beginning and end of the study.

21.4.1.1 If you've indicated that data is being collected via a device or application (e.g. FitBit, Apple Watch, eye tracker, etc.), will the developer/external entity have access to the research data?

☐ No

☒ Yes

Abbott will have access to the de-identified data collected via Abbott Freestyle Libre Pro System. The sensor collects blood glucose data and it is downloaded using a Reader by study staff. The data will be transmitted from the Reader to the LibreView cloud platform. This system is encrypted to prevent unauthorized access.

The developer of the Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool will have access to the collected de-identified data (see attachment ASA24 Data Security & Confidentiality Information).

21.4.2 Specify the level of data that will be stored electronically (refer to definitions at the top of this section – links to levels/storage: https://security.psu.edu/awareness/storage/

☐ Level 1 (e.g. public data, de-identified)
☒ Level 2 (e.g. identifiable)
☐ Level 3 (e.g. PHI, SSN)
☐ Level 4 (e.g. Classified data)

21.4.3 Indicate where the electronic data associated with this research study will be stored (Check all that apply)

21.4.3.1 PSU - Penn State University and Commonwealth Campuses

- Penn State IT provided database application:
  - ☒ Penn State REDCap
  - ☐ Penn State Qualtrics
  - ☒ Penn State, College, or Department IT managed file server, OneDrive, or SharePoint
  - ☐ Penn State GoogleDrive

- Other – Specify the database application or server:
  - ☒ Provide details about the data security features or attach security documentation provided by sponsor or group.

Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool: Respondent data are protected using industry standard security controls. All data entered into the ASA24 system at the respondent's computer are encrypted by the internet browser (e.g., Chrome, Firefox, etc) while transmitted to ASA24 servers using Secure Socket Layer (SSL) Technology. SSL allows for the authentication of the sending and receiving computers. Only a particular study's investigator(s) and the ASA24 operations team can access response data. Access is gained through usernames and strong passwords (see attachment ASA24 Data Security & Confidentiality Information).

CGM: The sensor collects blood glucose data and it is downloaded using a Reader. The data will be transmitted from the Reader to the LibreView cloud platform. This system is encrypted to prevent unauthorized access.

Please visit datastoragefinder.psu.edu for assistance with identifying appropriate data storage options. If the software to be used does not appear on that site, a software request form must be completed.

21.4.3.2 PSH/COM - Penn State Health/College of Medicine

- Penn State IT provided database application:
  - ☐ Penn State REDCap
  - ☐ Penn State Qualtrics
  - ☐ Penn State Health, College of Medicine, or Department IT managed file server
  - ☐ Office365, OneDrive, or SharePoint
    - Specify the O365 tenant to be used (PSU, PSH)

  - ☐ Oncore (Penn State Cancer Institute only)
  - ☐ Florence eBinders
  - ☐ External Institution's REDCap
  - ☐ Web-based system provided by the sponsor or cooperative group via contract

- Other – Specify the database application or server:
  - ☐ Provide details about the data security features or attach security documentation provided by sponsor or group.

21.5 Will any type of recordings (e.g., audio or video) or photographs of the subjects be made during this study or will you interact with subjects via live video streaming(video chat)?

☐ No – skip to 21.6
☐ Yes – Live video chat ONLY without recording. If this is the ONLY box checked, complete 21.5.1 only.
☒ Yes – Recording (audio, video, photographs, recording of video chat). If this is the ONLY box checked, skip to 21.5.2:

21.5.1 Select the video chat platform:

☐ PSH HIPAA Compliant Teams
☐ PSU Zoom
☐ Other: Specify:
[Type text here if box is checked]

21.5.2 Select the type of recording or image being made and what is being used to record or capture the image:

☐ Audio – Describe what will be used to capture the audio:
[Type text here if box is checked]

☐ Video – Describe what will be used to capture the video:
[Type text here if box is checked]

☒ Photographs of the subjects – Describe what will be used to photograph the subjects and whether facial images will be captured or collected:
[Participants will be asked to take photos with their smart phones of saliva sample vials immediately after sample collection. The purpose of these photos is to capture a digital timestamp for the sample collection time for compliance with with recommended guidelines for salivary cortisol[26]. These photos may include the participant's hand, but will not include facial images. Participants have been instructed not to include their faces in the image. Images will be uploaded to REDCap by study staff during sample return.]

☐ Recording of video chat
  - ☐ PSH HIPAA Compliant Teams
  - ☐ PSU Zoom

☐ Other: Specify:
[Type text here if box is checked]

☐ Other - Specify:
[Type text here if box is checked]

21.5.3 Will any of the recordings be transcribed?

Note: If a transcription service outside of Penn State will be used, a business associate agreement or data transfer agreement may be needed.

☐ No
☐ Yes – indicate who will be doing the transcribing? (Ex: Zoom, Rev.com, Datagain, 3Play Media). If necessary, please clarify if the transcription service is HIPAA compliant or not.

[Type protocol text here]

21.5.4 Will the recordings be destroyed or cleaned (removed of all identifiers)? If so, describe below.

[Type protocol text here]

21.6 Certificate of Confidentiality (COC) - Is the research biomedical, behavioral, clinical or other research that is funded by the National Institutes of Health (NIH)?

☐ Yes – this means at least one of the following is true:
- The research involves human subjects as defined by the DHHS regulations (See Worksheet
- HRP-310).
- The research involves collecting or using biospecimens that are identifiable to an individual.
- If collecting or using biospecimens as part of the research, there is a small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.
- The research involves the generation of individual level, human genomic data.

Note: If <u>any</u> of the 4 items above are true, a COC is automatically issued by NIH and applies to the research. Information about the COC must be included in the consent form.

☒ No - answer the following question.
If the research is not funded by NIH, will the investigator apply for a COC for this research study?
☒ No
☐ Yes

Note: For research not funded by NIH, the IRB may require a COC if the research is collecting personally identifiable information and the information is sensitive and/or the research is collecting information that if disclosed could significantly harm or damage the subject.

21.7 Does this research involve the generation of large-scale human genomic data as defined in NIH Genomic Data Sharing Policy (https://sharing.nih.gov/genomic-data-sharing-policy))?

☒ No
☐ Yes – describe the plan for de-identifying the dataset before sharing it with NIH-designated data repositories.

[Type protocol text here]

Note: Data sharing with an NIH-designated data repository may require execution of an institutional certificate. Please review the 'Institutional Certification for NIH Genomic Data Sharing' section of the Investigator's Manual for information about seeking institutional certification.

21.8 Does this research involve data sharing to public/restricted data repositories or as part of a journal requirement?

Data sharing is an important part of rigorous scientific discovery and the validation of results. Planning for data sharing is *strongly recommended*. Please refer to: https://libraries.psu.edu/about/departments/research-informatics-and-publishing/services/data-management-and-sharing

Data sharing includes sharing of identifiable, coded, or de-identified data. The data can be shared with public or restricted data repositories. Increasingly, journals require the sharing of data as a stipulation for publication. NIH-funded studies **require data sharing**, unless explicitly granted an exception from the NIH.

☐ No – skip to section 21.9
☒ Yes (*strongly recommended* as may be required for publication and future grant submission)

21.8.1 What type of data will be shared: De-identified, coded, identifiable (if identifiable, list the identifiers that will be shared)

☒ De-identified
☐ Coded (there is a study code ID being sent, but no identifiers with the study code)
☐ Identifiable – Specify the identifiers that will be shared:

De-identified data will be uploaded to a public data repository.

21.8.2 What type of repository will be used to share the data: Public, controlled, etc. Note: The specific name of the repository is not necessary.

Public

21.9 Does this research involve transfer or disclosure of data and/or specimens to and/or from Penn State?

☐ No - skip to section 22.0
☒ Yes - answer the following questions:

21.9.1 Specimen and/or data are being transferred or disclosed (electronically or physically) **TO** Penn State. Please insert study information in first blank row. Please add additional rows as necessary for each individual entity, do not have more than one entry in a row. (Example provided in grey)

Sharing Entity (if international, specify country)	Data or Specimen Type	Method of Transfer	Storage Location	Identifiers (Refer to table 1 in 21.1)	Linking List Location	Additional notes, if needed.

Quest Diagnostics	Screening blood results	Online platform Quanum Lab Services Manager	REDCap, CRC, Chandlee Lab	Name, screening study code, date of birth	n/a	Identifiers are included on screening bloods so that participants can provide these blood results to their medical clinic and/or primary care physician. The tests we do at screening are typical blood tests done for general health evaluation and therefore prospective participants often use these results for their annual physicals. This is viewed by participants as a benefit as it saves them the cost associated with paying for routine general health blood tests. If a study code was used for the blood results, it is likely that some medical clinics and/or physicians would not

						accept the results.
Self-Administered 24-Hour (ASA24®) Dietary Assessment Tool, NCI	Dietary data	Online platform: https://asa24.nci.nih.gov/	Onedrive	Study code	REDCap Onedrive	
Abbott	Continuous glucose data	Online platform: LibreView: https://www.libreview.com/	REDCap Onedrive	Study code	REDCap Onedrive	

21.9.2 Specimen and/or data are being transferred or disclosed (electronically or physically) **FROM** Penn State. Please insert study information in first blank row. Please add additional rows as necessary for each individual entity, do not have more than one entry in a row. (Example provided in grey)

Sharing Entity (if international, specify country)	Data or Specimen Type	Method of Transfer	Storage Location	Identifiers (Refer to table 1 in 21.1)	Linking List Location	Additional notes, if needed.
EXAMPLE: US based or International based Institution name (if international, specify country)	Consent forms, questionnaires, activity data from FitBit, liver biopsy sample, biopsy results, audio recordings.	Aspera, Office 365, REDCP, Sponsored platform/location	REDCap, Lab, CRC	Study code, Date of birth	☐ ONLY with External Entity ☐ External Entity and Penn State ☒ Penn State ONLY	
Quest Diagnostics	Blood	Quest carrier picks up the blood from the CRC	n/a	Name, screening study code, date of birth	n/a	Identifiers are included on screening bloods so that participants can provide these blood results to their

						medical clinic and/or primary care physician. The tests we do at screening are typical blood tests done for general health evaluation and therefore prospective participants often use these results for their annual physicals. This is viewed by participants as a benefit as it saves them the cost associated with paying for routine general health blood tests. If a study code was used for the blood results, it is likely that some medical clinics and/or physicians would not accept the results.

UP/Commonwealth Data Transfer:
Office of Sponsored Programs - Data transfers or disclosures may require a Data Use Agreement (DUA). If the third party is requiring us to sign a contract regarding the data, this contract must go through the Office of Sponsored Programs https://www.research.psu.edu/osp/overview-pages/data-use-agreements.

PSU/Commonwealth Material Transfer:
Office of Technology Transfer - All material transfers, either sending or receiving, require a Material Transfer Agreement (MTA). Please contact the Office of Technology Transfer for more information. https://ott.psu.edu/

Penn State Health/College of Medicine Data transfer:
Office of Research Affairs - Data transfers or disclosures may require a Data Use Agreement (DUA). If the Office of Research Affairs has not yet been contacted, please email e-contracts@pennstatehealth.psu.edu. If a third party is requiring us to sign a contract regarding the data, the contract must go through the Office of Research Affairs. Please submit at the following link: https://pennstatehershey.tfaforms.net/267.

Penn State Health/College of Medicine Material transfer:
Center for Medical Innovation - All material transfers, either sending or receiving, require a Material Transfer Agreement (MTA). If a MTA Intake Form has not been completed for this material transfer, please go to https://pennstatehershey.tfaforms.net/744 and complete the on-line MTA intake form. If you have any questions, please email CMI@pennstatehealth.psu.edu.

22.0 Identifiable Data and Specimen Banking for Future Undetermined Research

If this study is banking **identifiable** data and/or specimens that will be banked for **future undetermined research**, please describe this process in the sections below. This information should not conflict with information provided in the above sections regarding whether or not data and/or specimens will be associated with identifiers (directly or indirectly). If there are no plans to use identifiable data/specimens for future, undetermined research, then this section is **NOT applicable**.

[Do not type here]

22.1 Data and/or specimens being stored

Identify what data and/or specimens will be stored, and the data associated with each specimen.

Not applicable

22.2 Location of storage

Identify the location where the data and/or specimens will be stored.

Not applicable

22.3 Duration of storage

Identify how long the data and/or specimens will be stored. If data and/or specimens will be stored indefinitely, indicate such.

Not applicable

22.4 Access to data and/or specimens

Identify who will have access to the data and/or specimens.

Not applicable

22.5 Procedures to release data or specimens

Describe the procedures to release the data and/or specimens, including: the process to request a release, approvals required for release, who can obtain data and/or specimens, and the data to be provided with the specimens.

Not applicable

22.6 Process for returning results

Describe the process for returning results to participants from the banked data and/or specimens.

Not applicable