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).

Cardiometabolic effect of low-fat and full-fat dairy in healthy and cardio-metabolically at-risk adults

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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.

October 7, 2026

Clinicaltrials.gov Registration #:

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

NCT07605442

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

[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

2. **CATS IRB LIBRARY:**
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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:
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1.0 Objectives

1.1 Study Objectives

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

If the research will use or test Artificial Intelligence (AI), Generative AI, algorithms, machine learning, or deep learning, describe this. Include a detailed description of the technology(ies) to be used or tested and the intent of the research.

The overarching goal is to characterize and compare the effect of full-fat dairy to low-fat dairy on low density lipoprotein cholesterol (LDL-C) and other cardiometabolic disease (CMD) risk factors in healthy adults and those at risk for CMD. This goal will be achieved with the following objectives:

1. Characterize the effect of full-fat dairy compared to low-fat dairy on LDL-C and other CMD risk factors in healthy adults and adults at risk for CMD after 6 weeks.
2. Compare the effect of full-fat dairy to low-fat dairy in healthy adults vs. adults at risk for CMD after 6 weeks.

This clinical trial will test two hypotheses: 1) intake of 3 cup-equivalents/day of full-fat dairy (milk, yogurt & cheese) has equivalent effects on LDL-C and other CMD risk factors to 3 cup-equivalents/day of low-fat dairy (milk, yogurt & cheese) in adults with normal BMI and optimal/near optimal LDL-C, and in adults with overweight/obesity and elevated LDL-C after 6 weeks; 2) the effect of full-fat dairy on LDL-C and other CMD risk factors, compared to low-fat dairy, is equivalent in adults with normal BMI and optimal/near optimal LDL-C compared to adults with overweight/obesity and elevated LDL-C after 6 weeks. This trial is expected to demonstrate equivalent effects of full-fat and low-fat dairy on LDL-C and other CMD risk factors in both healthy and at-risk adults.

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).

LDL-C

1.3 Secondary Study Endpoints

State the secondary endpoints to be measured in the study.

Apolipoprotein B (apoB)
Triglycerides
Total cholesterol
HDL-cholesterol
Non-HDL-cholesterol
Fasting glucose and insulin
Fructosamine
Insulin resistance assessed by the homeostatic model of insulin resistance (HOMA-IR)
C-reactive protein (CRP)
Body weight
Central and peripheral blood pressure

Carotid femoral pulse wave velocity (PWV)
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.

Current dietary guidance for dairy: Dietary guidance issued by federal agencies and authoritative organizations for general health and cardiovascular disease (CVD) risk reduction recommends intake of low-fat or fat-free dairy rather than full-fat dairy.[1–4] This recommendation is made because of cardiovascular concerns about the higher saturated fat content of full-fat dairy as well as the higher energy content. However, observational and clinical trial evidence suggest that full-fat dairy intake is not associated with increased risk of CVD[5] or worsening of LDL-cholesterol (LDL-C),[6] a key risk factor for CVD. Although there has been limited empirical investigation of the cardiovascular implications of meeting dairy recommendations with full-fat dairy so concerns about population guidance to consume full-fat dairy instead of low-fat dairy remain. To address this evidence gap and inform population-level guidance for dairy intake, the goal of the proposed study is to determine if full-fat dairy has ***equivalent effects*** on LDL-C and other cardiometabolic disease (CMD) risk factors to low-fat dairy in both healthy adults and those at risk for CMD.

Epidemiological evidence for dairy intake and CVD risk: Prospective cohort studies generally show that higher total dairy intake is either not associated with CVD risk or associated with lower risk of CVD.[7] A recent systematic review and meta-analysis of 27 prospective cohort studies showed that higher total dairy intake was associated with an approximate 4% relative risk reduction for CVD, which equated to a 2% relative risk reduction per 1 daily serving increase in dairy.[5] A systematic review and meta-analysis of 24 prospective cohort studies published a few years earlier showed a similar relative risk reduction estimate, although it was not statistically significant (RR 0.96; 95% CI 0.92, 1.00).[8] In these analyses, dairy intake was estimated by diet assessment methods that are limited by measurement error. Recently, circulating and tissue levels of pentadecanoic acid (15:0) and heptadecanoic acid (17:0) have emerged as objective biomarkers of dairy intake. Notably, in a systematic review and meta-analysis of prospective cohort studies, high vs. low levels of 15:0 (RR 0.88; 95% CI 0.78, 0.99; 17 studies) and 17:0 (RR 0.86; 95% CI 0.79, 0.93; 12 studies) were associated with lower risk of total CVD.[9] Collectively, evidence from prospective cohort studies suggests that total dairy intake (or objective biomarkers of intake) is associated with either neutral or beneficial CVD outcomes.

Epidemiological evidence also suggests that higher vs. lower intake of full-fat dairy is either not associated with CVD risk or associated with lower risk.[7] There has been less investigation of the association between full-fat dairy relative to lower-fat dairy and CVD risk. The 2025 Dietary Guidelines Advisory Committee (DGAC) conducted a systematic review that included 9 prospective cohort studies (15 comparisons) and concluded that substituting higher-fat dairy with lower-fat dairy is not associated with a difference in risk of CVD in adults.[10] However, the evidence was graded as limited because of concerns with consistency, precision, risk of bias, directness, and generalizability. Thus, evidence from prospective cohort studies collectively suggests cardiovascular benefits of dairy intake regardless of the fat content.

Clinical trial evidence on the effect of dairy on CVD risk factors: Clinical trial evidence suggests that dairy intake, irrespective of the fat content, does not have adverse effects on anthropometric measures, lipids/lipoproteins, or blood pressure.[6] In a systematic review and network meta-analysis including 8 randomized controlled trials (RCT) with a duration ≥ 12 weeks, high intake of full-fat dairy (MD -7.60 mmHg; -17.18, 1.97) and low-fat dairy (MD -5.22 mmHg; 95% CI -10.01, -0.43) improved systolic blood pressure compared to a control/low dairy.[6] In these analyses, there was no effect of high dairy vs. low dairy (or dairy subtypes) on body weight, LDL-C, or triglycerides. Only a few clinical trials have examined the effect of full-fat dairy vs. low-fat/fat-free dairy on CVD risk factors.

Most clinical trials show no difference in blood pressure with full-fat dairy vs. low-fat dairy. [11–13] In a randomized crossover study of young adults who were normotensive (n=43), no difference in blood pressure (primary outcome blood pressure) was observed following intake of 3.5 servings/day of full-fat milk and yogurt, compared to low-fat milk and yogurt, after 8 weeks; however, body weight increased with full-fat vs. low-fat dairy.[11] In a 3-period randomized crossover study of generally healthy adults, a Dietary Approaches to Stop Hypertension (DASH) diet with full-fat dairy and lower in sugars reduced blood pressure compared to the control Average American diet, and to a similar extent as a DASH diet with low-fat dairy.[14] Collectively, clinical trial evidence suggests full-fat dairy has similar blood pressure effects to low-fat dairy.

Clinical trials have generally shown no difference in the effect of full-fat dairy vs. low-fat/fat-free dairy on lipids/lipoproteins.[12–15] In a 12-week RCT, there was no effect of intake of 80 g/d/2400 kcal of regular fat cheese vs. the same amount of low-fat cheese on LDL-C (primary outcome), total cholesterol, HDL-C, or triglycerides in participants at risk for CVD.[12] Similarly, another 12-week RCT conducted in adults with metabolic syndrome showed no effect of 3.3 servings/day of full-fat milk, yogurt, and cheese compared to the same amount of low-fat dairy or a limited dairy diet ≤3 servings/week on lipids/lipoproteins.[13] Therefore, despite the saturated fat content of full-fat dairy, the effect on lipids/lipoproteins does not appear to differ from low-fat dairy.

The milk polar lipid content of full-fat dairy may explain the neutral effect of full-fat dairy on LDL-C: The lack of effect of dairy fat on lipids/lipoproteins may be related to the structure of milk fat globules, which include a tri-layered membrane rich in bioactive phospholipids and proteins that enclose the milk fat.[7] In an 8-week RCT, intake of 40 g/day of whipping cream [contains milk fat globule membrane (MFGM)] resulted in lower LDL-C (-12 mg/dL; 95% CI -22, -1.5) than 40 g/day of butter oil in men and women with overweight or obesity.[16] However, this study was not able to identify the mechanism(s) for the attenuated lipid impairment associated with MFGM. In a 4-week randomized controlled trial, intake of 5 g/day of milk polar lipids reduced LDL-C, apoB, and triglycerides compared to the control (0 g/day) in postmenopausal women.[17] Furthermore, it was shown that the milk polar lipids reduced intestinal cholesterol absorption, resulting in a reduction in intestinal-derived chylomicrons and delivery of unabsorbed lipids to the colon. While further research is needed in this area, the available evidence suggests that the milk polar lipid content of full-fat dairy may explain the lack of adverse lipid/lipoprotein effects, supporting the biological plausibility of the non-different findings observed between full-fat and low-fat dairy in RCTs.

Clinical trial evidence on the effect of dairy on glycemic outcomes: RCT evidence suggests that there is no difference in the effect of full-fat dairy vs. low-fat dairy on markers of glycemic control.[12,15,18,19] Schmidt et al. observed no difference in the effect of 3.3 servings/day of full-fat vs. low-fat milk, yogurt, and cheese on glucose tolerance (primary outcome), systemic insulin sensitivity, pancreatic β-cell function, liver fat content, fasting glucose, HbA1c, and HOMA-IR after 12 weeks in adults with metabolic syndrome.[18] Similarly, in a randomized crossover trial (n=13), no difference in 120-minute glucose (following oral glucose tolerance test; primary outcome), glucose tolerance, fasting glucose or insulin, HOMA-IR, or insulin sensitivity was observed with intake of full-fat or non-fat yogurt in adults with prediabetes after 3 weeks.[19] In this study, fructosamine was lower after intake of full-fat yogurt

compared to non-fat yogurt. Thus, available RCT evidence suggests that full-fat and low-fat/non-fat dairy have similar effects on glycemic control.

2.2 Previous Data

Describe any relevant preliminary data.

See above for a summary of prior evidence. No relevant preliminary data are available.

2.3 Study Rationale

Provide the scientific rationale for the research.

Well-designed, adequately powered studies directly comparing the effect of low-fat and full-fat dairy on risk factors for CVD are needed to inform dietary guidance. The 2025 Dietary Guidelines Advisory Committee (DGAC) concluded that insufficient evidence exists to determine the effect of higher-fat dairy intake, compared to lower-fat versions, on blood lipids and blood pressure in adults and older adults.[20] Only 3 clinical trials[11,12,21] met the inclusion criteria for the DGAC systematic review.[10] Although, as described above, additional clinical trials exist, they were excluded because of small sample sizes (<30 participants/group). Under the current process for Dietary Guideline development, empirical evidence from adequately powered clinical trials demonstrating that full-fat dairy does not adversely affect cardiometabolic health, particularly lipids/lipoproteins, compared to low-fat dairy, will be needed to prompt any shift in recommendations.

All of the prior trials were designed to test for superiority rather than equivalence, i.e., full-fat dairy has a different effect than low-fat dairy on the outcomes of interest. Under the superiority testing framework, a non-significant difference (failure to reject the null hypothesis) is viewed as inconclusive and not as the same effect. Alternatively, a trial designed using the equivalence testing framework enables direct testing of the hypothesis that full-fat and low-fat dairy have the same effect. Given prior research suggests that full-fat dairy has similar effects on LDL-C and other CMD risk factors to low-fat dairy, directly testing whether these two types of dairy are equivalent would strengthen the evidence base and enable inferences to be drawn about the similarity of low-fat and fat-free dairy.

Dietary guidance is issued at the population level and therefore, evidence generalizability is important. Critically, most of the prior research on the effect of full-fat dairy vs. low-fat dairy was conducted in adults at risk for CVD or CMD, and research in healthy adults is limited. This is relevant because it is well established that excess adiposity impairs LDL-C responsiveness to dietary intervention.[22] Thus, individuals with overweight/obesity may respond differently to full-fat dairy vs. individuals with a healthy body weight. A direct comparison of full-fat vs. lower-fat dairy in both healthy and cardio-metabolically at-risk adults will inform population-level dietary guidance as well as precision public health recommendations.

The intent of this study is not to evaluate dairy's ability to cure, mitigate, treat, or prevent disease.

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.)

- Age 25-70 years
- BMI 18.5 to 39.9 kg/m^2
- LDL-C ≤190 mg/dL assessed by the Modified Sampson–NIH Equation
- Currently consume milk, yogurt, and/or cheese daily
- Willing to eat 3 servings of dairy (milk, yogurt, cheese) per day for two 6-week periods during the study

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 Iin your study.

- Hemoglobin <13.2 g/dL for men or < 11.7 g/dL for women 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
- Fasting glucose ≥126 mg/dL
- Type 1 or type 2 diabetes
- Takes any (prescription or over-the-counter) anti-hypertensive, lipid-lowering, glucose-lowering or anti-inflammatory drugs, or drugs that alter body weight
- Intake of supplements that affect the outcomes of interest (i.e., lipids, blood pressure, glucose, body weight, inflammation and microbiome) 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

Washout prior to baseline visit:
4-weeks for probiotics, fermented drinks, vitamins, and omega-3 supplements ≤2g/day and 6-weeks for omega-3 supplements >2g/day

- 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
- 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
- Dairy 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
- 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 3 servings of dairy/day during the study
- Lactose intolerance or sensitivity
- 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 (< 0.4 or >4.5 mIU/L), or change in dose of thyroid medication within the last 6 months
- Principal Investigator discretion related to the potential participant's ability to adhere to the study requirements, including being able to come to attend visits

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 or drugs that affect body weight (assessed by review of medical history form or participant report)
- Prescription of steroids, antibiotics or anti-inflammatory drugs 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 to ensure removal of decedents. It is the study team’s responsibility to ensure removal of decedents from the provided data.

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. Websites (e.g., http://clinicaltrials.gov/, Facebook/Instagram, 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 (see

attachment canned email to interested individuals) with additional study information and a link to the pre-screen survey (see attachment 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 Participants).

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 prescreening 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). In 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 provides consent, they will receive an email to schedule their telephone screening with Calendly, an online appointment scheduling tool (see attachment Canned Email to Individuals Eligible for Telephone Screening Part Two). Individuals not eligible for telephone screening based on their responses to the pre-screening survey will be notified by email (see attachment Canned Email to Individuals Not Eligible for Telephone Screening).

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 Procedure Consent Form). The research team member conducting the telephone screening will be in a private area.

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. Individuals selecting to receive their eConsent via email, will be emailed a copy of the completed econsent form (see attachment Canned econsent email).

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 List all material that will be used to consent and inform potential subjects about the research (e.g., a letter accompanying a questionnaire, verbal script, or implied consent form)

The Attachment HRP 585 Screening Procedures 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 "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 Subjects who are not yet adults (infants, children, teenagers)

Refer to "HRP-416 -CHECKLIST- Children" for information about research involving children as subjects.

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, remove the statement and indicate as not applicable.

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 randomized cross-over clinical trial with 2 parallel arms (see Figure 1). Arm 1 will include adults with normal BMI (18.5-24.9 kg/m^2) and optimal/near optimal LDL-C (≤ 129 mg/dL) and Arm 2 will include adults with overweight/obesity (25-39.9 kg/m^2) and elevated LDL-C (130-190 mg/dL. Within each arm, participants will undergo two 6-week dietary conditions in random sequence order, separated by a 4-week washout: 1) 3 cup-equivalents/day of full-fat dairy; 2) 3 cup-equivalents/day of low-fat dairy. All dairy will be provided and participants will have to visit the Penn State Research Kitchen weekly to pick-up the dairy foods.

Outcomes will be assessed at the start and end of each period (6 weeks ± 3 days). At the baseline (day 0 and 1) and 6 weeks (day 42 & day 43; ± 3 days) of each period, two blood samples will be collected for endpoint analysis (separated by approximately 24 hours). 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 on 2 days prior to baseline and during week 6 using 24-hour recalls (4 recalls per period). Participants will also provide a fecal collection at baseline and 6 weeks for each period.

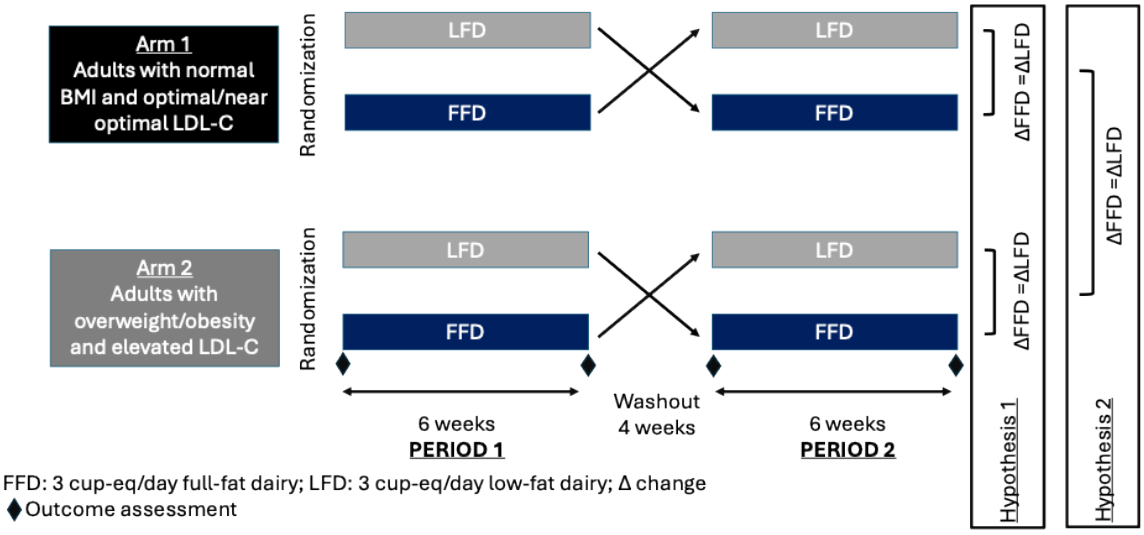


Figure 1: Study Design

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.)

[Do not type here]

7.2.1 Visit 1 Screening

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 at the time their clinic screening appointment is scheduled (see attachment Clinic Screening Appointment Confirmation Email). An email reminding the participant about their screening visit will be sent prior to their appointment (See attachments Clinic Screening Appointment Reminder).

At the clinic screening visit (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 with a calibrated electronic scale while the participant is wearing light clothing without shoes. Height will be measured using a stadiometer. 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 tablespoon 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, and uric acid. 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 approximately 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 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: Baseline Period 1 Day 1 Testing (B1.1)

Five days prior to visit 2, participants will receive an email asking them to complete several surveys (see attachment Canned Email_Baseline_Endpoint Survey Completion; the attachment ASA24-DietAssessmentInstructionSheet will be attached to the email). First, participants will be asked to review their medical history form (see attachment Medical History Form) 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.

Participants will also be asked to complete two 24-hour dietary recalls during the 5 days prior to the study visit to estimate their usual dietary intake. 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 as well as to assess food and nutrient intake. Participants will receive an email with instructions and log in information for completing two 24-hour dietary recalls (see attachments Canned Email_Baseline_Endpoint Survey Completion; ASA24-DietAssessmentInstructionSheet). Participants who do not complete the two recalls prior to Visit 2 will be asked to complete one recall at Visit 2 and one recall at Visit 3. A reminder to complete

the recalls will be included in the Visit 2 appointment reminder email sent 3 days prior to Visit 2 (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

Finally, 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), and stress (see attachment Perceived Stress Scale Survey). If participants do not complete these surveys prior to Visit 2, they will be asked to complete them during the Visit 2.

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 is designed to assess stress exposure.

The visit will be conducted according to the Baseline Data Collection Form (see attachment Data Collection Form_Period 1 Baseline.docx); 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.

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 taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to Visit 3. If participants are not able to complete a fecal collection between Visit 2 and Visit 3, 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.

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. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1 mL 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, 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 at Visit 2 and asked to bring the collected sample to Visit 3; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the participant. 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 and functionality (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.

7.2.3 Visit 3: Baseline Period 1 Day 2 Testing (B1.2)

Visit 3 will occur approximately 24 hours after Visit 2. At Visit 3, a fasting blood sample will be collected and PWA and PWV measurements will be taken if they were not completed at Visit 2 for any reason. Body weight will be taken. The fecal sample collection will be brought to the visit by the participant. If the participant has not completed all of their 24-hour 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 this 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 by the kitchen manager. The randomization sequence will have block sizes of 2, 4, and 8 and be computer-generated by a person not involved in recruitment or data collection and loaded into REDCap to conceal allocation. The randomization schedule will be stratified. Strata 1 will be for participants with a normal BMI (18.5-24.9 kg/m^2) and optimal/near optimal LDL-C (≤ 129 mg/dL). Strata 2 will be for participants with overweight/obesity (25-39.9 kg/m^2) and elevated LDL-C (130-190 mg/dL).

Participants will be provided with a map and directions to the Research Kitchen (See attachment Research Kitchen Directions and Parking). At the Kitchen, participants will be informed of which type of dairy they will receive first (low-fat or full-fat) and be provided with an instruction sheet (see attachments Full Fat Dairy Instructions; Low Fat Dairy Instructions). Participants will be asked to consume 1 cup-equivalent of milk (i.e. 244 g), yogurt (i.e. 244 g) and cheese (i.e. 40 g) each day. Participants will be provided with a 7 days' supply of dairy in single-serving portions. When they are in the full-fat condition they will receive whole milk, Fage 5% whole plain Greek yogurt, and regular Babybel cheese. When they are in the low-fat dairy condition, they will receive 1% milk, Fage 2% plain Greek yogurt, and reduced-fat Babybel cheese. Participants will be instructed to consume all of the provided dairy and use the provided dairy to replace dairy products usually consumed.

Every 7 days, participants will go to the Penn State Research Kitchen for the collection of dairy and adherence monitoring. Participants will receive daily adherence tracking surveys through SMS text messaging through REDCap (see attachment Daily Monitoring Text Message). Participants can opt out of text messaging at any time. If a participant opts out, they will complete a paper daily monitoring form for adherence tracking (see attached Daily Monitoring Form).

7.2.4 Visit 4: Endpoint Period 1 Day 1 Testing (E1.1)

Five days prior to Visit 4, participants will receive an email asking them to complete several surveys (see attachment Canned Email_Baseline_Endpoint Survey Completion; the attachment ASA24-Diet Assessment Instruction Sheet End of Periods will be attached to the email). First, participants will be asked to review their medical history form (see attachment Medical History Form) 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.

Participants will also be asked to complete two 24-hour dietary recalls prior to Visit 4 to estimate their usual dietary intake. 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 as well as to assess food and nutrient intake. Participants who do not complete the recalls prior to the visit will be asked to complete one recall at Visit 4 and one recall at Visit 5. A reminder to complete the recalls will be included in the Visit 4 appointment reminder email sent 3 days prior to Visit 4 (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

Finally, 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), and stress (see attachment Perceived Stress Scale Survey). If participants do not complete these surveys prior to Visit 4, they will be asked to complete them during the Visit 4.

The visit will be conducted according to the Endpoint Data Collection Form (see attachment Data Collection Form_Period 1 Endpoint); 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.

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 taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to Visit 5. If participants are not able to complete a fecal collection between Visit 4 and Visit 5, 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.

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. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1 mL 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, 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 at Visit 4 and asked to bring the collected sample to Visit 5; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the participant. 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 and functionality (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.

7.2.5 Visit 5: Endpoint Period 1 Day 2 Testing (E1.2)

Visit 5 will occur approximately 24 hours after Visit 4. At Visit 5, a fasting blood sample will be collected and PWA and PWV measurements will be taken if they were not completed at Visit 4 for any reason. Body weight will be taken. The fecal sample collection will be brought to the visit by the participant. If the participant has not completed all of their 24-hour 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 this 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 this visit, participants will have a washout period of ≥4 weeks.

7.2.6 Visit 6: Baseline Period 2 Day 1 Testing (B2.1)

Five days prior to Visit 6, participants will receive an email asking them to complete several surveys (see attachment Canned Email_Baseline_Endpoint Survey Completion.docx; the attachment ASA24-DietAssessmentInstructionSheet will be attached to the email). First, participants will be asked to review their medical history form (see attachment Medical History Form) 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.

Participants will also be asked to complete two 24-hour dietary recalls prior to Visit 6 to estimate their usual dietary intake. 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 as well as to assess food and nutrient intake. Participants who do not complete the recalls

before the visit 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 sent 3 days prior to the visit (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

Finally, 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), and stress (see attachment Perceived Stress Scale Survey). If participants do not complete these surveys prior to Visit 6, they will be asked to complete them during the Visit 6.

The visit will be conducted according to the Baseline Data Collection Form (see attachment Data Collection Form_Period 2 Baseline); 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.

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 taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to Visit 7. If participants are not able to complete a fecal collection between Visit 6 and Visit 7, 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.

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. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1 mL 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, 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 at Visit 6 and asked to bring the collected sample to Visit 7; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the participant. 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 and functionality (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.

7.2.7 Visit 7: Baseline Period 2 Day 2 Testing (B2.2)

Visit 7 will occur approximately 24 hours after Visit 6. At Visit 7, a fasting blood sample will be collected and PWA and PWV measurements will be taken if they were not completed at Visit 6 for any reason. Body weight will be taken. The fecal sample collection will be brought to the visit by the participant. If the participant has not completed all of their 24-hour 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 this 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 to collect their dairy. At the Kitchen, participants will be informed of which type of dairy they will receive (low-fat or full-fat) and be provided with an instruction sheet (see attachments Full Fat Dairy Instructions; Low Fat Dairy Instructions).

Every 7 days, participants will go to the Penn State Research Kitchen for the collection of dairy and adherence monitoring. Participants will receive daily adherence tracking surveys through SMS text messaging through REDCap (see attachment Daily Monitoring Text Message). Participants can opt out of text messaging at any time. If a participant opts out, they will complete a paper daily monitoring form for adherence tracking (see attached Daily Monitoring Form).

7.2.8 Visit 8: Endpoint Period 2 Day 1 Testing (E2.1)

Five days prior to Visit 8, participants will receive an email asking them to complete several surveys (see canned email Canned Email_Baseline_Endpoint Survey Completion.docx; the attachment ASA24-Diet Assessment Instruction Sheet End of Periods will be attached to the email). First, participants will be asked to review their medical history form (see attachment Medical History Form) 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.

Participants will also be asked to complete two 24-hour dietary recalls prior to Visit 8 to estimate their usual dietary intake. 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 as well as to assess food and nutrient intake. Participants who do not complete the recalls prior to the visit will be asked to complete one recall at Visit 8 and one recall at Visit 9. A reminder to complete the recalls will be included in the Visit 8 appointment reminder email sent 3 days prior to Visit 8 (See attachment Canned Email_Baseline_Endpoint Appointment Reminder).

Finally, 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), and stress (see attachment Perceived Stress Scale Survey). If participants do not complete these surveys prior to Visit 8, they will be asked to complete them during the Visit 8.

The visit will be conducted according to the Endpoint Data Collection Form (see attachment Data Collection Form_Period 2 Endpoint); 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.

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 taken. Participants will be given a fecal collection kit and asked to collect a sample at home and bring it to Visit 9. If participants are not able to complete a fecal collection between Visit 8 and Visit 9, 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.

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. A typical American Red Cross blood donation is 1 pint (500 mL). Plasma/serum will be aliquoted (~0.5-1 mL 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, 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 at Visit 8 and asked to bring the collected sample to Visit 9; if an individual is not able to collect the sample within this timeframe, alternative arrangements will be made to accommodate the participant. 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 and functionality (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.

7.2.9 Visit 9: Endpoint Period 2 Day 2 Testing (E2.2)

Visit 9 will occur approximately 24 hours after Visit 8. At Visit 9, a fasting blood sample will be collected and PWA and PWV measurements will be taken if they were not completed at Visit 8 for any reason. Body weight will be taken. The fecal sample collection will be brought to the visit

by the participant. If the participant has not completed all of their 24-hour 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 this 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.

This study involves 2 six-week study periods with a ≥4-week break between the period. Following screening it may take up to 3 months for an eligible person to start the study.

The screening visit will take approximately 1 hour. The testing visits will take approximately 1 hour on day 1 and approximately 30 minutes on day 2. The screening visit, and 8 testing visits will take approximately 7 hours. Each 24-hour recall will take approximately 20 minutes (2 hours, 40 minutes for 8 recalls). The surveys will take approximately 10 minutes to complete at each time point (40 minutes for surveys at 4 timepoints). Weekly visits for dairy pickup and adherence monitoring will take approximately 15 minutes (3 hours for 12 visits). Therefore, this study will involve approximately 13 hours and 20 minutes.

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, 75 participants need to complete each arm of the study. Therefore, a total of 150 participants need to complete the study. It is expected that 178 participants will be randomized to achieve 75 completers in each arm. To randomize this number, it is expected that 534 participants will sign a consent form and be 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.

For the first hypothesis, 75 subjects per group are needed to test within-group equivalence in the 6-week change in LDL-C (primary outcome), assuming a between-condition mean difference of 0 mg/dL (SD 14.6 based on a prior study from our lab looking at a single food intervention in a similar population[23]), an equivalency margin of ±5 mg/dL, 80% power, and $p<0.05$. An equivalency margin of 5 mg/dL is used because a change in LDL-C of <5 mg/dL is not associated with a clinically meaningful change in ASCVD risk.[24] Furthermore, prior studies comparing full-fat dairy to low-fat dairy show effect estimates of -0.8 to 3.1 mg/dL.[12–15] 75 subjects per group will also provide adequate power to test the

second hypothesis; the same equivalency margin will be used for the second hypothesis. Overall, 150 subjects are needed; 178 subjects will be recruited to account for an ~15% attrition rate.

8.3 Statistical or Analytic Methods

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

The primary analysis will include all data collected from randomly assigned participants consistent with intent-to-treat principles. A secondary per-protocol analysis will be conducted that will only include participants with a high level of adherence defined as consuming ≥ 90% of the provided dairy (≥2.7 cup-equivalents/day) on ≥90% of the study days (≥ 38 days). This will be treated as a sensitivity analysis to determine the robustness of the findings. Assumptions for all statistical tests will be checked and confirmed prior to conducting analyses for hypothesis testing. The change from baseline will be calculated by subtracting the endpoint value from the baseline value for each condition. To test hypothesis 1, within-arm (Arm 1 and Arm 2) equivalency for all outcomes will be tested using paired samples t-tests with two one-sided tests (TOST) for equivalence. Equivalence will be established if the 90% confidence interval for the mean difference falls entirely within the predefined equivalence bounds. Equivalency margins for all outcomes will be defined based on clinical importance. For hypothesis 2, between-arm (Arm 1 vs. Arm 2) equivalency will be tested using independent samples t-tests with TOST equivalence analysis. The same equivalency margins will be used for hypotheses 1 and 2. Statistical significance $p<0.05$.

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 dairy products; 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 dairy allergy may manifest during the study. This is most likely to occur within the first week of the study. We ask participants to please inform study staff should any adverse events occur.

Food Preparation
Dairy products will be purchased from local stores or food delivery services and portioned into single 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 or secure platform such as REDCap. 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.

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, and uric acid at no cost.

11.2 Potential Benefits to Others

Describe the potential benefits to society or others.

The results to contribute to understanding how the fat content of dairy impacts health. It is expected that the study findings will be used by federal agencies and authoritative organizations when making population-level recommendations about the type of dairy to consume for general health.

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 CRC Nurse Practitioners or Physicians) and asked to schedule a visit with their primary care provider.

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 (check or direct deposit) up to $400 as compensation for the time and burden associated with participating in

the study. Payment will be made following Visit 9. Payment will be prorated as follows for partial completion.
Participation in visits 2 and 3 = $30
Participation in visits 4 and 5 =$40
Participation in visit 6 and 7 = $130
Participant in visits 8 and 9 = $200

Participants may not be eligible for compensation if determined that specific work or visa laws conflict.

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 on-going 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.).

Not applicable

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 lead investigator 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.

1. U.S. Department of Agriculture, U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. Published 2020. Accessed January 1, 2021. www.dietaryguidelines.gov
2. Lichtenstein AH, Appel LJ, Vadiveloo M, et al. 2021 Dietary Guidance to Improve Cardiovascular Health: A Scientific Statement From the American Heart Association. *Circulation*. 2021;23(144):e472-487.
3. Kirkpatrick CF, Sikand G, Petersen KS, et al. Nutrition interventions for adults with dyslipidemia: A Clinical Perspective from the National Lipid Association. *J Clin Lipidol*. 2023;17(4):428-451.
4. Jones DW, Ferdinand KC, Taler SJ, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: a Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. Published online 2025. doi:10.1016/j.jacc.2025.05.007
5. Zhuang P, Liu X, Li Y, et al. A global analysis of dairy consumption and incident cardiovascular disease. *Nat Commun*. 2025;16(1):437.
6. Kiesswetter E, Stadelmaier J, Petropoulou M, et al. Effects of dairy intake on markers of cardiometabolic health in adults: a systematic review with network meta-analysis. *Adv Nutr*. 2023;14(3):438-450.
7. Torres-Gonzalez M, Bradley BHR. Whole-milk dairy foods: biological mechanisms underlying beneficial effects on risk markers for cardiometabolic health. *Adv Nutr*. 2023;14(6):1523-1537.
8. Chen Z, Ahmed M, Ha V, et al. Dairy product consumption and cardiovascular health: a systematic review and meta-analysis of prospective cohort studies. *Adv Nutr*. 2022;13(2):439-454.
9. Trieu K, Bhat S, Dai Z, et al. Biomarkers of dairy fat intake, incident cardiovascular disease, and all-cause mortality: A cohort study, systematic review, and meta-analysis. *PLoS Med*. 2021;18(9):e1003763.
10. Gardner C, Hoelscher D, Tobias D, et al. *Food Sources of Saturated Fat and Risk of Cardiovascular Disease: A Systematic Review*.; 2024. Accessed September 4, 2025. https://doi.org/10.52570/NESR.DGAC2025.SR24
11. Alonso A, Zozaya C, Vázquez Z, Alfredo Martinez J, Martinez-Gonzalez MA. The effect of low-fat versus whole-fat dairy product intake on blood pressure and weight in young normotensive adults. *J Hum Nutr Diet*. 2009;22(4):336-342.
12. Raziani F, Tholstrup T, Kristensen MD, et al. High intake of regular-fat cheese compared with reduced-fat cheese does not affect LDL cholesterol or risk markers of the metabolic syndrome: a randomized controlled trial. *Am J Clin Nutr*. 2016;104(4):973-981.
13. Schmidt KA, Cromer G, Burhans MS, et al. Impact of low-fat and full-fat dairy foods on fasting lipid profile and blood pressure: exploratory endpoints of a randomized controlled trial. *Am J Clin Nutr*. 2021;114(3):882-892.
14. Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. *Am J Clin Nutr*. 2016;103(2):341-347.
15. Engel S, Elhauge M, Tholstrup T. Effect of whole milk compared with skimmed milk on fasting blood lipids in healthy adults: a 3-week randomized crossover study. *Eur J Clin Nutr*. 2018;72(2):249-254.
16. Rosqvist F, Smedman A, Lindmark-Månsson H, et al. Potential role of milk fat globule membrane in modulating plasma lipoproteins, gene expression, and cholesterol metabolism in humans: a randomized study. *Am J Clin Nutr*. 2015;102(1):20-30.
17. Vors C, Joumard-Cubizolles L, Lecomte M, et al. Milk polar lipids reduce lipid cardiovascular risk factors in overweight postmenopausal women: towards a gut sphingomyelin-cholesterol interplay. *Gut*. 2020;69(3):487-501.
18. Schmidt KA, Cromer G, Burhans MS, et al. The impact of diets rich in low-fat or full-fat dairy on glucose tolerance and its determinants: a randomized controlled trial. *Am J Clin Nutr*. 2021;113(3):534-547.
19. Taormina VM, Eisenhardt S, Gilbert MP, Poynter ME, Kien CL, Kraft J. Full-fat versus non-fat yogurt consumption improves glucose homeostasis and metabolic hormone regulation in individuals with prediabetes: A randomized-controlled trial. *Nutr Res*. 2025;136:39-52.

20. 2025 Dietary Guidelines Advisory Committee. *Scientific Report of the 2025 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and Secretary of Agriculture*.; 2024. Accessed December 15, 2024. https://doi.org/10.52570/DGAC2025
21. Nilsen R, Høstmark AT, Haug A, Skeie S. Effect of a high intake of cheese on cholesterol and metabolic syndrome: results of a randomized trial. *Food Nutr Res*. 2015;59(1):27651.
22. Flock MR, Green MH, Kris-Etherton PM. Effects of adiposity on plasma lipid response to reductions in dietary saturated fatty acids and cholesterol. *Adv Nutr*. 2011;2(3):261-274.
23. Hart TL, Kris-Etherton PM, Petersen KS. Consuming Pecans as a Snack Improves Lipids/Lipoproteins and Diet Quality Compared to Usual Diet in Adults at Increased Risk for Cardiometabolic Diseases: A Randomized Controlled Trial. *Am J Clin Nutr*. 2025;121(4):769-778.
24. Silverman MG, Ference BA, Im K, et al. Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. *JAMA*. 2016;316(12):1289-1297.

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 laptops or 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.

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

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/icdt/

☐ 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.

  Please visit 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, a software request form must be completed.

  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).

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:
[Type text here if box is checked]

☐ 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/	Onedriv e	Study code	REDCap Onedriv e	

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)

Receiving Entity	Data or Specimen Type	Method of Transfer	Domestic / International Destination	Identifiers (Refer to table 1 in 21.1)	Linking List Location	Additional notes, if needed.

EXAMPLE: Institution name	Consent forms, questionnaires, activity data from FitBit, liver biopsy sample, biopsy results, audio recordings.	Aspera, Office 365, REDCP, Sponsored platform/location	☒ Domestic (US Based Destination) ☐ International Destination (specify country)	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 at Penn State that will be used 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