Gut Microbiota Dependent and Independent Impacts of Dietary Pulses on Pre- and Postprandial Metabolism and Inflammation in Overweight/Obese Humans

NCT04283448

Informed Consent

Study Document Date: 06/22/2022

SUBJECT CONSENT FORM FOR PARTICIPATION IN HUMAN RESEARCH AT MONTANA STATE UNIVERSITY

Study Title: Impact of Diet and Gut Microbiome on Metabolism and Inflammation

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Summary:

You are being asked to volunteer as a participant in a research study of how different foods influence health, the microorganisms that live in the gut (bacteria), and other molecules (metabolites) produced during chemical reactions in the body. There are many different kinds of bacteria that are in the gut. These bacteria and other organisms in your gut are called the 'gut microbiome', and they differ in their effects on the body. These microorganisms have the potential to influence health because they influence inflammation, responses to the ingestion of dietary fat, control of blood sugar, obesity, and other factors that influence how likely individuals are to develop diabetes, cardiovascular diseases, and other diseases. The types and quantities of carbohydrate, fat, protein, and fiber in foods can influence how the food affects the bacteria in our gut and our health. Similarly, sedentary and physical activity behaviors can influence these same factors. We are specifically interested in how different foods affect people who have higher levels of a particular type of fat, called triglycerides, in the blood. We will do a test to see if you have high triglycerides and, if you do, we will have you complete the rest of the study. If you do not have high triglycerides, you will not complete any further activities in the investigation.

Purpose:

The purpose of this study is to determine how certain food items may affect gut bacteria, molecules (metabolites) produced during chemical reactions in the body, inflammation, and the metabolic health of individuals with an increased waist circumference and non-fasting triglyceride (the main fat in your blood) levels in the blood. A second purpose of this study is to test how changes in the gut microbiome influence how people respond to dietary changes. Specifically, we are asking the following questions:

1) How do specific foods in your diet affect metabolism, inflammation, your responses to a high-fat meal, and the bacteria in your gut?
2) How do diet-induced bacterial changes in your gut relate to inflammation, responses to a high-fat meal, and other measures related to health?
3) How do sedentary and physical activity behaviors influence diet, bacteria in your gut, metabolism, inflammation, and health?

If we learn how food influences the bacteria in our gut and how that may influence our health, then we can use that information to do more research to improve the health of people in a future study.

Participants in the study:

You have been asked to participate in this study because you meet the following criteria: 18-70 years of age, with a waist circumference greater than 35 inches for women and 40 inches for men. You may not be a participant if you do not meet eligibility requirements of our screening questionnaire because of health history, symptoms, issues or risks, if you have an allergy to wheat or dairy, if you are taking medications to lower cholesterol, lipids, and/or inflammation, if you are pregnant, have diabetes, have a pacemaker, or if you have other health concerns or conditions that may interfere with your participation in the study. You may also be excluded if you are planning a weight loss diet or a change in exercise regimen.

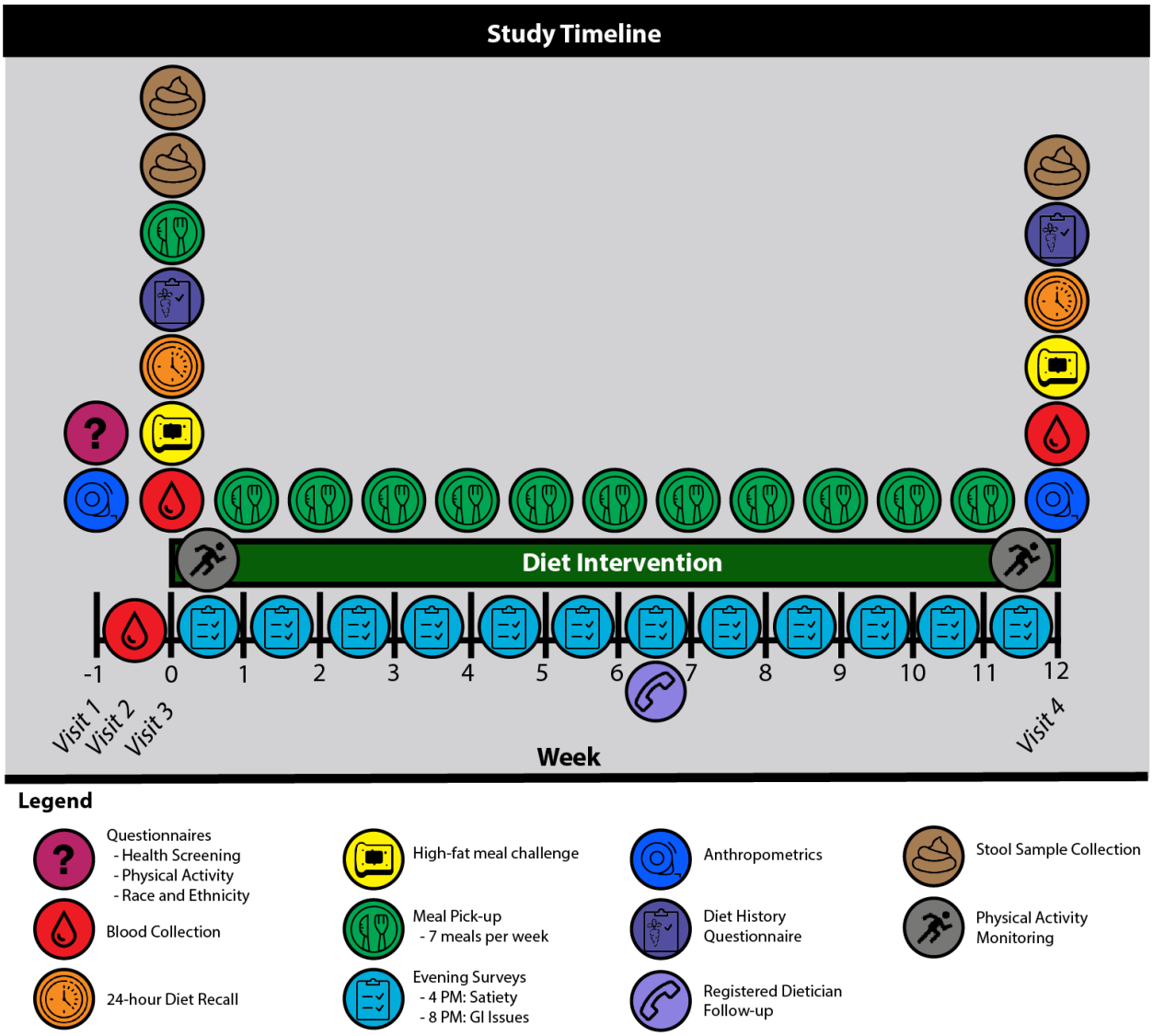
Procedures:

Participation is voluntary. If you agree to participate in this study, you will be asked to complete four visits to the Nutrition Research Laboratory to complete the procedures of the investigation and an additional 6-12 brief exchange appointments (depending on how many meals you can or prefer to store in your home freezer) to pick up food for the study. An initial visit (Visit 1) will take 45-60 minutes. Visit 2 will last less than 60 minutes and consist of coming to the laboratory for collection of a single blood sample (~ 1 teaspoon) to measure the levels of triglycerides in your blood. If your triglycerides are greater than 175 mg/dl at this visit, then we will ask you to continue with the remainder of the study. If your triglycerides are not greater than 175 mg/dl, then we will thank you for your participation and stop with the study procedures.

The third (Visit 3) and fourth (Visit 4) visits will take approximately 6 hours each and will each include 6 blood draws through a blood sampling catheter, with each blood draw collecting about 2-3 teaspoons of blood. Blood will be drawn before a meal of toast and butter, then hourly for 6 hours after meal consumption. There are 12 weeks between visits 3 and 4. During the 12 week period, you will be asked:

- To consume food provided to you by researchers at your midday meal for each day of the week, including weekend days
- To make an effort to control portion sizes at your evening meal
- To complete a total of two 24-hour dietary recalls that require about 30 minutes of your time each when prompted by researchers
- To complete brief (less than two minutes) online or smartphone questionnaires two days per week when prompted by researchers

Completion of the study will take approximately 13 weeks, depending on scheduling of the visits. Total time spent in the Nutrition Research Laboratory is approximately 14 hours. A visual overview of the study is provided at the top of the next page.



Visit 1: This visit will take 45 to 60 minutes and include the following activities:

1) **Informed consent.** Read and provide written informed consent (this form). We also will provide you with a copy of this form and discuss it with you prior to proceeding with any additional activities in visit 1.
2) **Health screening questionnaire.** Complete a health history questionnaire that asks questions about your health and the health of your family, particularly regarding heart disease.
3) **Physical activity questionnaire.** Complete a 3-question survey that asks questions about the types and amount of physical activity that you typically perform during the week.
4) **Race and ethnicity questionnaire**. Complete a 2-question survey that asks questions about your ethnicity and race. This survey is optional. Your information will not be used for analysis of race and ethnic differences.

5) **Body size measurements.** The researcher will take baseline measurements of height, and circumferences of your waist. You will remain clothed during these measurements; however, you will be asked to remove extra clothing items such as coats or sweatshirts.
6) **Measurement of muscle and fat tissue using bioelectrical impedance analysis.** This test simply involves standing on a scale with your feet and hands on sensors for a few seconds. A very low electrical current that you cannot feel and that is not dangerous is transmitted and received across the sensors. The technology is commonly used in a variety of settings such as gyms and health screenings, but the instrument that we will use is more sophisticated in being able to estimate muscle and fat tissue in different regions of your body, including the abdominal cavity that is particularly important for predicting risk of diabetes.
7) Instructions and supplies will be given for **self-collection of a stool sample**. A stool sample will be used to analyze the microbes in your gut. The analysis involves measurement of the genetic material of the bacteria. This does not give us any information about your genetic material, only that of the bacteria in your gut. You will be given three self-collection kits that each come with printed instructions to collect your stool sample. Specimen will be collected and brought to the lab when you come for visits 2, 3, and 4 (or as soon as possible after this visit).

Visit 2. This visit will take place 3-4 hours after you have consumed a meal (breakfast or lunch) that contains approximately 50 g of fat. Investigators will discuss an appropriate meal for you to eat prior to this visit and schedule a time for this visit. The visit will take no more than 60 minutes and include the following activities:

1) **Informed consent.** Due to length of the study, we will revisit the informed consent (this form) to discuss study activities and to answer any questions you might have. Read and provide written informed consent to continue the study.
2) **Blood collection**. Blood will be drawn from a forearm vein one time according to standard procedures. The blood collected will be measured for triglyceride levels immediately after the blood collection. If the level of triglycerides is greater than 175 mg/dl, then you will continue with the study. If the level of triglycerides is lower than 175 mg/dl, then you do not qualify for the intervention of the study and your participation in the study will end.

Visit 3 and 4 (separated by 12-week dietary intervention): You will need to refrain from eating, exercising, and consuming alcohol for 12 hours prior to each visit. You should drink plenty of water so that you are well hydrated throughout the study. Each visit will take approximately 7 hours and include the following activities:

1) **Informed consent.** Due to length of the study, we will revisit the informed consent (this form) at the beginning to discuss study activities and to answer any questions you might have. Read and provide written informed consent to continue the study.
2) **Resting blood pressure measurement**. Two measures of blood pressure will be taken with a standard blood pressure cuff.
3) **Blood collection.** Standard procedures for collection of blood from a forearm vein will be used to collect blood. A trained phlebotomist or physician will clean your skin with an iodine-based solution or alcohol and place a catheter needle in a vein in the front part of

your elbow (most common), forearm, or hand. The catheter needle (20 gauge or 18 gauge) is slightly larger than what is used for venous punctures (21 gauge), but smaller than what is typically used in blood donations (16 gauge). A small amount of a sterile salt solution (saline) will be put into the catheter to keep the line open for the collection of blood samples. Blood samples will allow us to measure the following values: glucose and HbA1c (a measure that reflects your average glucose level for the previous 90 days), lipid panel, inflammatory markers, and metabolites (a wide variety of small molecules relating to all of the biochemical processes in your body).

4) **High fat meal tolerance test.** After the line has been in your arm for 15 minutes, we will begin the test by measuring your blood pressure on the arm without the venous catheter, collecting a fasting blood sample, and then having you eat a meal consisting of toast and butter with water, and then collecting blood through the catheter each hour for the next six hours. We will keep the arm with the catheter warm during the test and ask you to squeeze a foam ball in your hand a few times a minute to help keep blood flowing to your arm. If blood collection is not possible through the catheter toward the end of the test, then we will ask you whether you want us to complete the test by drawing blood with a needle stick using the standard blood collection method. You can stop at any time during this test. You will have limited ability to use a laptop computer, cell phone, or read during this test. When the test is completed, the catheter will be taken out of your arm. We will have you keep pressure on the site where the catheter was for 5-10 minutes. We will have some food in the lab so that you can eat before leaving the lab. This food is for your comfort and not part of the test so you can choose the foods that you want.
5) **Diet History Questionnaire.** An online questionnaire that will ask you about the frequency and quantity of foods consumed in your diet. This questionnaire will go through food groups and different times of year prior to the study (Visit 3) and the last month of the study (Visit 4) to estimate of the types and amounts of nutrients that you typically consume in your diet. This questionnaire takes 1-2 hours to complete, but you will be able to complete this at the same time you are conducting the high fat meal tolerance test.
6) **24-hour diet recall obtained.** An online 24-hour diet recall will outline the types and quantities of foods and beverages consumed the day prior.
7) **Portion size and intuitive eating strategies video.** An online video outlining the importance of portion sizes and intuitive eating strategies will be viewed during this visit. Practicing intuitive eating will help you to mindfully tune into your body's hunger and satiety cues. At the end of the video, you will be asked five questions to check your knowledge and understanding. The video and questionnaire will take 10-15 minutes to complete, but you will be able to complete this at the same time you are conducting the high fat meal tolerance test.

12-Week Dietary Intervention:

1) **Weekly meals.** Seven meals per week to be consumed as the midday meal will be provided to the participants either weekly or biweekly, depending on their preference. Eat as much of each meal as possible to comfortable level of fullness. Record anything not eaten or if additional food was eaten to achieve desired level of fullness.

2) **Portion size**. Participants will be asked to pay close attention to the portion sizes of their evening meals, as well as their level of fullness, and to stop eating at or before feeling full.
3) **Weekly questionnaires**. Participants will be asked to respond to questions regarding their feelings of satiety/hunger and GI discomfort/comfort each week. Participants will receive these questionnaires via text message or email, according to individual preference, at 4:00 pm for satiety/hunger and 8:00 pm for GI discomfort.
4) **Physical Activity Monitor**. Participants will also be asked to maintain their normal level of physical activity throughout the duration of the study. You will be asked to wear an activity monitor for 7 consecutive days in the first and twelfth week to record your daily physical activity. We will ask that you wear the activity monitor during waking hours each day and to maintain usual activity habits during this time period. You will also be asked to maintain a log of your daily activity during each period of 7 days. The log will include indicating when you take the activity monitor off and put it back on. You will also record activity that you did during each day (e.g., walked for 30 minutes or watched TV for 1 hour).
5) **End-of-study questionnaire**. During visit 4, participants will be asked to complete a brief questionnaire about their experience during the study.

Physician review of your data: After you have completed the study, you will receive the results of your blood tests in a written report. A physician, Dr. Sarah Bronsky, will review your data and provide feedback in the written report. If appropriate, she will discuss results with you directly to help you understand how the measurements relate to your health and whether any follow up with your personal physician is recommended.

Risks: There are side effects and risks involved from having blood drawn or doing certain activities. These side effects are often called risks, and for this project, the risks are:

1) An intravenous needle/plastic catheter will be placed in your arm for the removal of blood samples and infusion of fluids. This will be left in for approximately 6.5 hours. Approximately 12 milliliters or 2-3 teaspoons of blood will be removed on 5 occasions during the high fat meal tolerance test. You can expect to experience some pain at the moment the needle/needle containing the plastic catheter goes into your arm. In addition to this momentary pain, there will be minor discomfort of having the catheter taped to your skin. In about 10% of cases, a small amount of bleeding under the skin will produce a bruise (hematoma). The risk of temporary clotting of the vein is about 1%, while the risk of infection of hematoma or significant external blood loss is less than 1 in 1,000. Some people may feel lightheadedness, nausea, or perhaps faint.
2) The high fat meal may make some people feel nauseous and may even vomit. You can stop at any time.
3) There is the possibility of gastrointestinal disturbance (flatulence) as a result of this diet.
4) Bacteria from the stool sample can cause illness if ingested. This risk is no different than when you normally empty your bowels. Washing your hands thoroughly with soap and hot water after collection of the sample will minimize this risk.

Benefits: You may gain some benefits by participating in this study, such as body composition, blood pressure, fasting blood glucose, and blood lipid panel. No other benefits are promised to you.

Biospecimens: Your samples will be used for analysis on hundreds of different metabolites. Metabolomic and inflammation analysis may take up to 2 years to complete and are not stored or banked for other analyses.

Compensation: You will receive up to $250 upon completion of your testing, $25 for each of the first two visits, $100 each for visits 3 and 4. You may withdraw from the study at any time. If you choose not to complete a condition, then the amount of money paid to you will be prorated depending on how much of the condition is completed.

Freedom of Consent: You have the right to withdraw from participating in the study at any time with a no questions asked policy. You may withdraw in writing, over the phone (to Mary Miles at 994-6678), or in person. If you withdraw, you will not lose any benefits you incurred up to the time of withdrawal. Your participation in this study is completely voluntary.

Funding: This study is funded by the USDA ARS Pulse Crop Health Initiative.

Please ask any questions: You are encouraged by the researcher to ask any and all questions you may have, as well as addressing any concerns about the study. The researcher will answer your questions as fully and as accurately as possible. Your peace of mind and comfort in the study is of utmost importance to the researchers.

Confidentiality: All data and information received from you for this study will be kept completely confidential. You will be given a subject identification number that will be used to describe all data. This data will be kept locked in a file cabinet in the Nutrition Research Laboratory. This information could be published in scientific and/or medical journals, but your identity will remain confidential. If you withdraw from the study at any time, all of your information will be deleted from the study records, and you will not be contacted again regarding the study. There are absolutely no penalties for withdrawing.

In the unlikely event of injury to you due to participation in this study, medical treatments such as first aid and help getting to adequate health care providers (such as transport to Bozeman Deaconess Hospital) will be provided, however, there is no compensation for any of this provided by Montana State University. You can access further information involving this policy and treatment by contacting Mary Miles at 994-6678, or emailing her at mmiles@montana.edu.

Any other questions you may have regarding your rights as a participant may be answered by the chairman of the Human Subjects Committee, Mark Quinn. He can be reached at 406-994-4707 or mquinn@montana.edu.

STATEMENT OF AUTHORIZATION

Study Title: Impact of Diet and Gut Microbiome on Metabolism and Inflammation

AUTHORIZATION: I have read the above and understand the discomforts, inconveniences, and risk of this study. I, _____(name of subject), agree to participate in this research. I also agree that my health information can be collected and used by the researchers and staff for the research study described in this consent form. I understand that I may later refuse participation and that I may withdraw from the study at that time. I have received a copy of this consent form for my own records.

VISIT 1

Signed: _____ Date: _____

Investigator: _____ Date: _____

VISIT 2

Signed: _____ Date: _____

Investigator: _____ Date: _____

VISIT 3

Signed: _____ Date: _____

Investigator: _____ Date: _____

VISIT 4

Signed: _____ Date: _____

Investigator: _____ Date: _____