Permission to Take Part in a Human Research Study

AdventHealth Orlando
Translational Research Institute for Metabolism and Diabetes

Title of research study: **Integrating Quantitative Energetics Determines the Microbiome's Contribution to Energy Balance**

IRBNet #: 942699

Sponsor's Name: **AdventHealth Orlando**

Investigator: **Steven R. Smith, MD**

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

We invite you to take part in a research study because you meet the following requirements:

- Age 18 – 45 years
- BMI ≤ 30 kg/m2
- Good general health

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.
- If you are an employee of AdventHealth Orlando, you should know that your participation or lack of participation in this study will not affect your employment or relationship with AdventHealth Orlando.

Why is this research being done?

You are being invited to participate in a research study because you are a healthy man or woman between 18 and 45 years of age and are stable in weight. A clinical trial (research study) is done when researchers (investigators) are trying to discover what works in medicine. A member of the research team will discuss the study with you. Please ask the study doctor or the study staff to explain words or information you do not understand. Understanding this study's risks and benefits will allow you to make an informed choice about whether to be part of this research study. This process is called informed consent. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. You should not sign this document until you understand

all of the information presented in the following pages and until all of your questions about the research have been answered to your satisfaction.

The purpose of this study is to collect data to examine how diet impacts the composition and function of the bacteria in your large intestine. This community of bacteria is called the gut microbiome. Recent evidence suggests that these bacteria are important for determining how many of the calories you eat are absorbed. Several studies have shown an association between the bacteria in your large intestine and diseases like obesity and diabetes. This study will improve our understanding of how diet may be able to lead to a healthy gut microbiome.

How long will the research last?

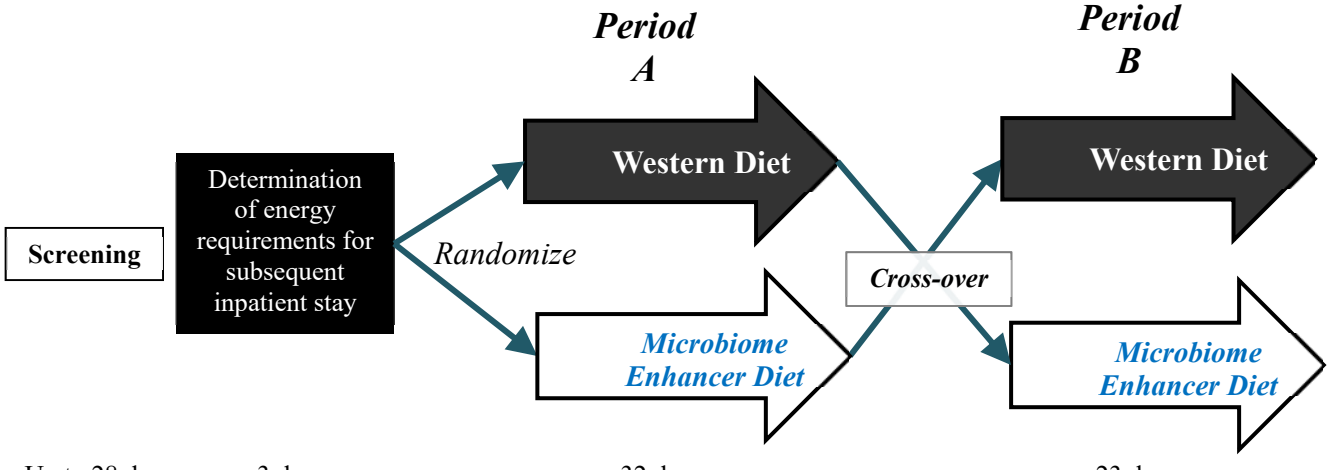
The overall study duration for each participant is approximately 90 days: a 28-day screening period, a 3-day period to collect data that will determine calorie requirements, and two dietary intervention periods: the first is 32 days and the second is 23 days (with a period of up to 14 days in between in most cases). During the diet periods, there will be 13 overnight stays. All visits are completed at The Translational Research Institute for Metabolism and Diabetes (TRI-MD).

How many people will be studied?

This study is only being conducted at AdventHealth Orlando Translational Research Institute for Metabolism and Diabetes (TRI-MD). The study will include healthy men and women that are stable in weight. Approximately 18 participants will be enrolled during this study. The study will consist of all ethnic categories and roughly equal numbers of men and women.

What happens if I agree to be in this research?

This is a crossover design where all participants will consume both diets (Western diet and Microbiome Enhancer diet) in random order. The study team will give you the diet in the order required. The picture below shows the overall timeline of study visits.



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Biospecimens will be collected. Biospecimens are materials taken from the human body, such as blood, that can be used for research. The following biospecimens will be collected for this research study:

- Blood
- Urine
- Stool

Once collected for this study, your biospecimens will become the permanent property of AdventHealth Orlando and the Translational Research Institute for Metabolism and Diabetes (TRI-MD).

If you agree to take part in this study, you will first sign this Informed Consent Form (ICF) before any study related procedures are performed.

After signing this Informed Consent Form, you will undergo an initial screening process to determine if you are eligible to participate in this study. We will ask about any changes in health history and medications at every visit.

Study Restrictions:

- If you decide to be in this study, you may have to stop taking some medications as needed, such as dietary supplements/herbals or substances that could affect metabolism, as well as oral nutritional beverages and nutritional supplements that might modulate body weight or aid in weight loss. You will be asked to stop taking these medications/beverages/ supplements during your screening visit and you will be asked to not take them over the entire course of the study.
- No alcohol allowed during outpatient feeding periods
- Please abstain from alcohol for 48 hours prior to Period B
- Caffeine containing products (with nothing added) will be permitted during the study with the following restrictions: caffeine containing products may not be consumed within 72 hours prior to admission.
- You may consume beverages of your choice that are calorie free such as water, black coffee (no cream/milk, sugar or artificial sweeteners), or other calorie-free beverages ***without*** artificial sweeteners such as unsweet iced tea, herbal tea, or black coffee. If you have other beverage preferences, please speak to study staff.
- Use of tobacco and nicotine-containing products is not permitted in this study.
- Please abstain from strenuous exercise (eg, heavy lifting, weight training, calisthenics, aerobics) for at least 48 hours prior to each admission. Walking at a normal pace will be permitted.
- Please maintain usual physical activity in between visits.

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Screening Visit, Day -28 to Day -1: ~2 hours (Fasting 10 hours- nothing to eat or drink except water for the 10 hours prior to visit):

The screening visit will include:

- **Medical History.** You will be asked about your medical history, which will include questions about any active or past diagnoses you may have.

- **Bowel Health Questionnaire.** You will be asked questions about your bowel history.

- **Antibiotic Use Questionnaire.** You will be asked questions about your antibiotic history.

- **Medication and Supplement Use.** We will ask you about all of the medications and supplements you have taken or are currently taking. If you decide to be in this study, you may have to stop taking some medications as needed, such as dietary supplements/herbals or substances that could affect metabolism, as well as oral nutritional beverages and nutritional supplements that might modulate body weight or aid in weight loss. You will be asked to stop taking these medications/beverages/ supplements during your screening visit and you will be asked to not take them over the entire course of the study.

- **Physical Measurements.** We will measure your vital signs (respiratory rate, temperature, blood pressure and heart rate), height, and weight. Prior to your weight being taken, you will be asked to empty your pockets, remove your shoes, and remove any heavy outer garments. Your Body Mass Index (BMI) will be calculated. BMI is a measurement of body fat based on height and weight that applies to adult men and women. We will also measure your waist and hip circumference using a measuring tape.

- **Physical exam.** A standard physical examination will be performed by a study physician, physician assistant, or nurse practitioner.

- We will collect a **pregnancy test**, if you are female and able to have children. We will also perform a **urinalysis and toxicology screen**.

- **Blood Draw.** We will collect blood at TRI-MD in the morning, **fasting; meaning no food or drink for at least 10 hours before your visit time (you may drink water and take your regular medications as scheduled).** A small sample of blood, about 9 mls (~ 2 teaspoons), will be drawn from an arm vein. The tests that will be performed on your blood include a complete blood count with differential, comprehensive metabolic panel, HbA1C, TSH. Repeat blood samples may be required, per provider request.

Participants who are eligible based on this evaluation, will be scheduled for Day 1.

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Visit 1/ Day 1 (outpatient, ~ 2 hours) +/- 2 day window: You will arrive for this outpatient visit and will have the following performed:

- **Physical Measurements.** We will measure your vital signs (heart rate, temperature, blood pressure, and respiratory rate).

- We will collect a **pregnancy test**, if you are female and able to have children.

- **DEXA (Dual energy X-ray absorptiometry).** You will have a measurement of your body's fat and muscle content. This is a non-invasive scan called a dual-energy x-ray absorptiometry or "DEXA" scan. This scan is performed similar to an x-ray study. You will lie on an examination table in a room equipped with the DEXA scanner. There are no contrast injections (x-ray dye) or blood samples. The test is painless except for any discomfort you may experience in your back because of lying on the firm examination table. The DEXA Scan will take about 15 minutes. Females of childbearing potential will undergo urine pregnancy testing prior to the DEXA scan.

- **Armband/Wristband accelerometer.** You will have two activity monitors placed and will be asked to wear the monitors for 7 days, except while showering/bathing. The armband monitor will be worn around your upper left arm. The wristband monitor will be worn around the wrist. If you are allergic to nickel, please inform the study staff.

- A stool sample needs to be collected. This sample needs to arrive at TRI on frozen cold packs within 24 hours of collection. You will be asked to provide the stool sample on Visit 1 (Day 1). If not able to produce a sample, you will be provided with a stool specimen collection kit that includes all necessary supplies to collect the stool sample, a box with cold packs for transport and instructions for collection. You can collect the stool sample at home anytime between Day 1 and Day 9. Once produced, call the study coordinator to make arrangements for the sample to be dropped off. If the stool sample is produced on Day 7, you may bring it with you with the frozen cold packs to Visit 2 on Day 8. If the sample is produced on Day 9, you may bring the sample in during Visit 3 on Day 10. This stool sample will only be collected during Period A. If not produced, the participant may continue in the study.

Visit 2/ Day 8 (outpatient, ~ 30 minutes) +/- 2 day window: You will come to TRI-MD to have your armband/wristband accelerometers removed.

Visit 3-6 Day 10-20/ Visit 9-12 Day 39-49 (outpatient/inpatient):

- **Day 10/Day 39 (Outpatient Controlled Diet):** Breakfast will be consumed at TRI-MD up to 3 times per week. Lunch and dinner will be provided and consumed at home. You will be asked to consume 100% of each meal. You will consume this diet from days 10-20 and days 39-49. If you have any food not consumed from your meal, you will bring it back to TRI-MD.

You will receive a scale to record your daily weight and be allowed to keep the scale at the end of your participation in the study. The study staff will also provide you with a diary with instructions for you to write down your daily weight. You will obtain your body weight in the morning before eating and drinking and after emptying your bladder and bowels. Prior to taking your weight also remove all clothing. Remember to remain still while taking your measurements.

You will start taking an oral medication called Polyethylene Glycol (PEG). The purpose of using PEG in this study is to accurately measure the absorption of nutrients. You will take one capsule three (3) times daily with meals until the end of the study.

- **Day 11-13/ Day 40-42 (Inpatient):** You will arrive on Day 11/Day 40 after dinner time to be admitted to the TRI-MD Clinical Research Unit (CRU) for a 23 hour Metabolic Calorimetry stay. Your weight and vital signs will be taken during your inpatient stay.

  The 23 hour Metabolic Calorimetry stay is in a specialized room that measures the amount of oxygen that you use and the amount of carbon dioxide you produce. All urine will be collected while you are in the room. Meals will be consumed at specific time points to maintain consistency throughout the study. The food will be the same menus as the diet you were assigned to consume at home. You will wear two activity monitors while in the calorimeter. On Day 12/ Day 41, you will stay in our whole room calorimetry for about 23 hours. You will be discharged to go home on Day 13/Day 42 after you eat breakfast.

- **Day 14-20/Day 43-49 (Outpatient Controlled Diet):** You will return to the clinic up to 3 times to consume breakfast. Lunch and dinner will be provided to be consumed at home. You will bring any food that is not consumed back to TRI-MD. Your weight will be recorded at home daily.

  Polyethylene Glycol (PEG) one capsule three (3) times daily will be continued with meals until the end of the calorimeter study days (Day 29/Day 58).

Visit 7 Day 21 - 32/ Visit 13 Day 50-61(inpatient):

- **Day 21 through 23/ Day 50-52**-You will check into the TRI-MD to start your 11 day in-house visit. You will stay in our Clinical Research Unit to become aware and accustom to the unit and it's routine. Polyethylene Glycol (PEG) one capsule three (3) times daily will be continued with meals. On Day 52, a small blood sample (about 2 mls or half a teaspoon) will be taken to check your hemoglobin.
  The following procedures will be completed:
  - **Physical Measurements.** We will measure your weight, vital signs (heart rate, temperature respiratory rate, and blood pressure) daily.

- **DEXA (Dual energy X-ray absorptiometry) (Day 23/Day 52).** You will have a measurement of your body's fat and muscle content. This is a non-invasive scan called a dual-energy x-ray absorptiometry or "DEXA" scan. This scan is performed similar to an x-ray study. You will lie on an examination table in a room equipped with the DEXA scanner. There are no contrast injections (x-ray dye) or blood samples. The test is painless except for any discomfort you may experience in your back because of lying on the firm examination table. The DEXA Scan will take about 15 minutes. Females of childbearing potential will undergo urine pregnancy testing prior to the DEXA scan.

- **MRI/S-Body fat distribution, liver fat and organ size analysis (Day 23/ Day 52).** This test will measure the amount of fat inside your body and your liver, as well as the size of your organs. For this test, you may be asked to change into a hospital gown. If you've previously been instructed to wear comfortable, clothes without zippers or rivets, you may be allowed to remain in your clothes. You can also request to wear a hospital gown. You will be given hearing protection (ear plugs and ear phones) for the MR scans.

  You will lie on a table in the MR scanner, and lie as still as possible to measure the amount of fat in your liver. Once positioned on the table, you will be moved into the magnet. When the imaging begins, you will hear loud knocking noises. For several of the images, you will be asked to hold your breath for up to 20 seconds for several of the images. For the remainder of the images, you can breathe normally, but need to stay lying still. The entire MR procedure, including positioning on the table, preliminary guidance images and quantification of fat, will take up to an hour and a half.

  The results from these tests will not be meaningful in regards to your health or wellbeing as they cannot be used for diagnostic analysis. However, upon completion of the study, you may request a paper copy of your images acquired during the study. If your body size is larger than the opening of the scanner, it will not be possible to have an MRS scan.

- **Diet History Questionnaire (Day 22).** You will be asked to complete a questionnaire regarding the frequency of food you consumed over the last year. There will be approximately 140 questions and will take about an hour to complete.

- **Day 24-29/ Day 53-58 (inpatient whole room calorimetry):** You will spend a continuous 23 hours a day in a specialized room that measures the amount of oxygen that you use and the amount of carbon dioxide you produce. Fresh air is continuously

supplied to the small, comfortable room equipped with a toilet and sink with privacy screen, treadmill, bed, desk, telephone, and computer with access to television, internet, and other forms of entertainment. Food and fresh water are passed through an air-lock drawer system. For the proper measurement to occur, the door to the room must remain shut for the duration of the study. You can communicate through the intercom and see the nursing staff through a window. There is a device to measure your movement in the room and a camera linked to the nursing station to assure your safety. Members of the nursing staff will be present outside the room for the duration of the study. During the calorimeter stay, it is very important that you consume 100% of the foods provided. If you are unable to do so, all food ingested will be recorded, and unconsumed food will be weighed. Units of food will be provided to match any food not consumed. An exercise bout (walking on treadmill) will be done.

You will be allowed to exit the calorimeter for a shower for 1 hour each day, however, all urine and fecal material will be collected – if produced - while outside the calorimeter.

- **24-hour urine and fecal collection:** To better understand how your body uses different foods for energy, all urine and fecal matter will be collected over 24 hours for 6 days during your time in the Metabolic Chambers. The samples will be tested to measure the nutrient composition in human waste.

- **Physical Measurements.** We will measure your vital signs (respiratory rate, temperature, heart rate, and blood pressure).

- You will continue taking the oral medication called Polyethylene Glycol (PEG) three (3) times daily with meals until the final day in the calorimeter (Day 29/Day 58).

- **Radiotransmitter Pill.** You will swallow a small silicone coated capsule on one of the 6 days while in the whole room calorimeter. This capsule will wirelessly send a signal to a recorder worn on a belt clip or a lanyard to record your internal body (core) temperature, pressure and pH level for 23 hours while you are in the calorimeter. The capsule normally remains in the body for 24-72 hours and will be passed as you move your bowels.

On Day 58, if the Hemoglobin at Day 52 does not meet criteria, a repeat will be performed stat before the blood is drawn on Day 59.

- **Day 30/Day 59 (inpatient):** You will exit the whole room calorimeter and will have an IV inserted to collect fasting blood samples. If the intravenous catheter no longer gives

blood or is not able to be inserted, blood may be drawn directly from your veins to collect the samples. Routine metabolic measures including lipids, glucose, and insulin and hormone samples will be collected (18 samples over 24 hours) before and after meals. About 346 mls (1.4 cups) of blood will be taken. We will measure your vital signs (heart rate, temperature, respiratory rate, and blood pressure). Liquid acetaminophen will be administered by mouth to measure the emptying of stomach contents.

- **24-hour urine collection:** All urine produced over 24-h will be collected on day 30/59 to be aliquoted for specific endpoints related to energy balance, metabolism and enteroendocrine hormones.

- **Day 31/ Day 60 (inpatient):** You will have your IV removed and we will measure your vital signs (heart rate, temperature, respiratory rate, and blood pressure). Breakfast, lunch and dinner will be given. These meals will be served in a controlled environment and then consumed over 30 minutes in our food intake lab.

  Visual analogue scales (VAS) will be administered before and after meals to understand the perception of hunger using a set of questions. This will take less than 5 minutes per VAS.

  The following procedures will be completed:

  - **DEXA (Dual energy X-ray absorptiometry) (Day 31/ Day 60).** You will have a measurement of your body's fat and muscle content. This is a non-invasive scan called a dual-energy x-ray absorptiometry or "DEXA" scan. The DEXA Scan will take about 15 minutes. Females of childbearing potential will undergo urine pregnancy testing prior to the DEXA scan.

- **Day 32/Day 61 (inpatient/discharge from TRI-MD):** We will measure your vital signs (heart rate, temperature, respiratory rate, and blood pressure), and weight. You will be provided with a breakfast. You will then be discharged from TRI-MD and will return to your usual diet up to 14 days (this period may be extended if your hemoglobin is not normal when drawn at Day 38). If it is not normal, we will delay the start of the second diet period and you will return to TRI-MD again to have your hemoglobin checked. If it is normal, you will start again with Day 39 as stated above. After you complete two diet periods, your participation in this study will conclude.

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

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor/study staff.
- Tell the study doctor/study staff about any changes in your health or the way you feel.
- Tell the study doctor/study staff if you want to stop being in the study at any time.
- Tell the study doctor/study staff about any supplements/medications you are presently using.

The success of this research study depends, in part, on collecting all of the data from all of the participants who agree to be in the study. If there is missing data, then this can negatively affect the conclusions from the study. Before you sign this Informed Consent Form to take part in this research, it is very important that you understand that you will not be able to change your mind about giving the biospecimens for research after they have been collected. You will only be able to change your mind before the biospecimens are collected. Please take as much time as you need to think about this before agreeing to participate in this study.

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

Treatment may involve risks which are currently unforeseeable. This section will cover the potential risks we are aware of at this time. You will be informed in a timely manner of any significant new findings that develop during the investigation that may affect your willingness to continue in the study.

Inpatient Stay: There are no physical risks associated with the inpatient stay, however some participants may experience feelings such as restlessness, irritability and loneliness.

Study Diet: With a change in diet it is possible that participants will experience gastrointestinal (GI) symptoms on the one of the diets such as flatulence, cramping, diarrhea, or constipation.

Vital Signs/ Blood Pressure Testing: You may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff on your arm.

Intravenous Line (lab samples, e.g.) – There is a risk of pain, vasovagal syncope, hematomas, and/or infection at IV insertion (low risk). To protect against risk, all venipuncture will be conducted by qualified staff using aseptic techniques.

Blood draws: You will undergo needle sticks during visits where blood samples are collected. You may have pain, light-headedness, fainting, infection, bleeding or bruising at the site of injection; however the staff will use proper technique while taking blood samples in order to reduce the risk of these unwanted effects. You may feel hungry or weak during the times you are required to fast. The total amount of blood drawn during the study will be about 26 ounces

(about 3.2 cups) over a period of about 3 months. In comparison, the typical amount collected during a blood bank donation is one pint (2 ¼ cups).

Whole Room Calorimetry: The calorimeter in itself carries no risk during the measure of your metabolic rate in the whole room. There may be some risk associated with the activity being performed in the chamber. The only adverse factor about this testing may be a feeling of claustrophobia. A member of the study staff will be nearby at all times and will check to see that you are comfortable.

Armband/Wristband Accelerometry: There are no risks associated with the wearing of activity monitors. However, the armband that holds the monitors in place may be irritating to the skin for some participants. Participants with nickel allergies may have irritation at the site of the monitor.

Magnetic Resonance Imaging and Magnetic Resonance Spectroscopy: There are no known biological risks associated with magnetic resonance imaging. Some short-term discomfort may be experienced. The short-term risks associated with MRI/MRS are minimal, but include heating, loud noises and claustrophobia. There are some people who should not undergo MRI/MRS; the contraindication is largely based on the presence of metal objects within a person (i.e. pacemaker, aneurysm clip, metal fragments, etc.). There will be a strict safety screening protocol, to ensure any people with contraindications are excluded from volunteering.

> **INCIDENTAL IMAGING FINDINGS:** This study does not evaluate your medical health. However, as part of the study we will obtain images, and it is unlikely but possible that these images may show an abnormality. If such an abnormality is found, you will be directed to seek attention from your health care provider.

PEG: PEG is generally recognized as safe. Based on clinical studies with the doses used in this study there were no adverse events nor do we anticipate any problems. In much higher doses (17 grams) PEG is used to treat constipation. At these same (higher) doses – such as those used for constipation and prior to colonoscopy – PEG can cause loose, watery, more frequent stools, nausea, bloating, cramping or abdominal pain.

Acetaminophen: Allergic reactions (primarily rash, pruritic rash, and urticaria) or reports of hypersensitivity (including anaphylaxis) associated with acetaminophen are very rare and generally are controlled by discontinuation of the drug and, when necessary, symptomatic treatment.

Radiotransmitter pill: Previous GI surgery or certain GI disorders increases the risk of intestinal blockage. You will be excluded from the study if you have a history of certain GI disorders. Additional discomfort may be associated if you trouble swallowing large pills/vitamins.

DEXA (Dual Energy X-ray Absorptiometry): The risks associated with having a DEXA scan include exposure to radiation from the scan. The amount of radiation that you will be exposed to is very small, about the same amount you would receive from 3 1/2 days of background radiation from the sun, or less than a chest X-ray. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you are still concerned with the radiation exposure, you can discuss this with your physician. If you are pregnant, you should not have a DEXA scan performed, as the risks posed by these procedures to the fetus is unknown. Therefore, if you are a woman of childbearing potential, a urine pregnancy test will be done prior to the DEXA.

***Other Risks*:** In addition to the risks listed above, you may experience a previously unknown risk or side effect. You will be asked in advance about any previous injury, which could prevent you from participating in this test.

PREGNANCY: This research may involve risks to the embryo or fetus if you become pregnant. Specific risks are currently unknown. If you are pregnant or nursing a baby or intend to become pregnant during the study, you should not participate in the study and you should notify the investigator(s). If you become pregnant or you miss a period during the study, you should notify the research team. Acceptable methods of contraception include intrauterine device, spermicidal and barrier method (e.g., condom, diaphragm), oral contraceptives (birth control pills), and abstinence. Please discuss the best choice for you and your partner with your study doctor. You must undergo a pregnancy test to ensure you are not pregnant as part of the screening for this study.

Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include that knowledge may be gained that will benefit others. No promise can be made concerning the study outcome, because results from a clinical research study cannot be predicted. Your participation will help researchers obtain additional information on the predictors of health in the general population.

Are there any costs in this study?

The Translational Research Institute for Metabolism and Diabetes (TRI-MD) will provide the study diets free of charge during this study. The TRI-MD will pay for supplies and procedures that are specifically related to the study. Tests and procedures that are done only for the study will not be billed to you or your insurance company.

You or your insurance company may be billed for:

- Any standard medical care given during this research study.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include who will pay the costs of treating possible side effects.

Will there be compensation for injury?

In the event of research-related injury or illness, medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. The Translational Research Institute for Metabolism and Diabetes (TRI-MD) has no program to pay for medical care for research-related injury or illness.

If you are injured as a result of this study, the study doctor will review the situation and, if necessary, provide treatment or refer you for treatment.

If you have questions concerning your participation in this study or if at any time you feel you have experienced a research-related injury or a reaction to a study drug, contact:

Steven R. Smith, MD
Chief Scientific Officer, AdventHealth Orlando Research
Senior Investigator, Translational Research Institute
301 E. Princeton St.
Orlando, FL 32804
407-303-7100
Or
Research Study Coordinator
301 East Princeton Street, Orlando FL 32804
(407) 303-7100

What happens to the information collected for the research?

To the extent allowed by law, we limit your personal information to people who need to review it. We cannot promise complete secrecy. The Institutional Review Board (IRB) and other representatives of this organization may inspect and copy your information for the purpose of providing research oversight.

To help protect your confidentiality, your samples will be labeled with a coded number that is different from your clinic number. This number is used instead of your name to help protect your identity. The samples are then stored in a secure location in the TRI-MD laboratory until a scientist is ready to study them.

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For the purposes of this study, we may need to send some of your biospecimens and information to outside laboratories for analysis/testing that cannot be done at AdventHealth Orlando. If this is needed, provisions will be put in place to protect the confidentiality of your information.

After the purpose and aims of this study have been met, we will store any left-over or remaining biospecimen samples for additional or future testing that may be needed that could not be predicted at the time you signed the Informed Consent. It is often the case in the process of scientific discovery, we realize that an additional test(s) may help advance the answers we may find.

Also, we will store biospecimens for future research, testing, or experiments. The biospecimens will be stored indefinitely until a research need for them is identified. Because these biospecimens would be used for future research at AdventHealth Orlando and other research institutions, we cannot be sure exactly how they will be used. It is possible that biospecimen samples may be used for chemical, DNA, RNA or protein testing that help us understand the function of the body. Cells from the biospecimens may be separated and treated in various ways to better study them and how they work. Scientists are learning new things every day that may suggest future research directions. Although we cannot predict the exact types of future research, testing, or experiments that may be performed with your samples, there are measures in place to make sure that the research has scientific merit and that the use of your samples will be specifically for research that is similar to the purpose/aims of this research study

You can receive some of the clinical results from the testing if you request them.
Translational Research Institute for Metabolism and Diabetes (TRI-MD) have no provision for compensation, monetary or otherwise, to participants in a research study in the event of a commercial development from information/results gathered during a research study.

The sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.
A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
Federal law provides additional protections of your medical records and health information. See the HIPAA section below.

Can I be removed from the research without my OK?

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is in your best interest;

- you do not consent to continue in the study after being told of changes in the research that may affect you;
- you have not followed study instructions;
- the investigator has stopped the study;
- AdventHealth Orlando IRB or other administrative area of AdventHealth Orlando has decided to stop the study; or
- Administrative reasons require your withdrawal

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.
We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

This research is being funded by the National Institute of Health (NIH).

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him or her.
You should contact your study doctor at his/her office number, which is a 24-hour number, call 911, or go directly to an Emergency Room. If you have additional questions or concerns, call the Principal Investigator listed on page one of this document.

You will be told about any new information that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.
If you agree to take part in this research study, we will pay you up to $5000 for your time and effort. Participants in screening through end of Period A, who complete all scheduled procedures and visits will be paid $2560.00. If you withdraw from the study prior to completing all procedures, your payment will be prorated to the procedures you completed per the below schedule. Payments are made in the form of a check or an electronic funds transfer and may take up to 2 weeks to be processed, once requested**.**

<u>Screening through End of Period A:</u>
Screening- $50.00
Day 1, Day 8 and Outpatient Diets- $235.00
Determination of Calorie Needs- $350.00
Inpatient Testing Block- $1925.00
TOTAL: $2560.00

Participants in Period B who complete all scheduled procedures and visits will be paid $2,440.00. If you withdraw for the study prior to completing all procedures, your payment will be prorated to the procedures you completed per the below schedule. Payments are made in

the form of a check or an electronic funds transfer and may take up to 2 weeks to be processed, once requested***.***

Period B:
Outpatient Diets- $165.00
Determination of Calorie Needs- $350.00
Inpatient Testing Block- $1925.00
TOTAL: $2440.00

Study payments that reach/exceed IRS limits of $600.00 in a calendar year will be reported to the IRS as required by law.

HIPAA Authorization to Release Information for Research

If you have not received a copy of the AdventHealth Orlando Privacy Notice, please request one. If you have questions about your privacy rights, you may contact AdventHealth Orlando's Privacy Officer at PH: (407) 303-9659.

Privacy laws, including the Health Insurance Portability & Accountability Act (HIPAA) and other federal and state laws, rules, and regulations, protect your individually identifiable health information (also called Protected Health Information or PHI). If you agree to be in this study, privacy laws require you to sign this Authorization that describes your rights and explains how your Protected Health Information (PHI) will be used and disclosed for this research study. By signing this informed consent/HIPAA Authorization, you will be authorizing the principal investigator, his/her research staff, and the sponsor (see top of page one) to use (which includes reviewing your medical records as necessary to conduct the study) and disclose your PHI for the purposes described below. By signing this form, you will also be authorizing your doctors, AdventHealth Orlando personnel, and individuals who provide health care services at AdventHealth Orlando to disclose your PHI for the purposes described below. This includes information from your past, present, and future medical records.

This Authorization does not have an expiration date. This means the researchers and others associated with this study may use and disclose your protected health information for as long as necessary to complete the study.

If you volunteer to take part in this research study, others may learn your identity. Study information may identify you in the following ways.

- Name
- Address
- Telephone number
- Social Security Number (SSN will only be used to report study payment information to the IRS as required by law. No study information will be linked to your SSN).

Permission to Take Part in a Human Research Study

This study includes a number of researchers, businesses and government agencies. They may use your health information and share it with others. We want you to know who may use this information and how they may use it.

Who may use and give out information about you?
The Investigator (study doctor) and research staff will have information about your health that tells us your identity. They may give this information to others during and after the study.

Who may see this information?
The study sponsor may see your health information and know your identity. "Sponsor" includes people or companies working for or with the sponsor or owned by the sponsor.

In addition to the study sponsor and its agents, the following people, agencies and businesses may get information from us that identify who you are.

- Doctors and healthcare professionals taking part in the study;
- U.S. Department of Health and Human Services (DHHS), which includes:
  - U.S. Food and Drug Administration (FDA)
  - U.S. Office of Human Research Protections (OHRP)
- Government agencies that must receive reports, including reports about certain diseases
- Government agencies in other countries
- AdventHealth Orlando representatives
- Institutional Review Board (IRB)
- Accreditation organizations
- Publications, medical meetings, or scientific journals (individual patients will not be identified).

What information may be used and shared?
If you decide to be in this study, medical information that identifies you and relates to your participation will be created, used, and/or shared. This may include the following types of medical information.

- Information obtained from procedures used to find out if you are eligible to take part in this study. This may include physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information that you may release to us, including information about your health history.
- Information from your medical chart.
- Information obtained in the course of the study including information about your response to any study treatments you receive, information related to study visits and phone calls, physical examinations, blood and urine tests, x-rays and other tests or

procedures that may be performed, and other medical information relating to your participation in this study.

Why will this information be used and/or shared?
Information about you and your health, that might identify you, may be given to others to carry out the research study. The sponsor and/or the investigator will analyze and evaluate the results of the study. In addition, if this is a sponsored study (see page one) people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

What if I decide not to give permission to use and give out my health information?
If you sign this consent form, you will be giving permission to use and give out the health information listed above for the purposes described above. If you decide not to give permission, you will not be able to be in this research. However, this will not change your relationship with your doctor or with AdventHealth Orlando and you will still be able to receive all benefits to which you are entitled.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this authorization (permission) will never expire (end) unless you revoke (cancel) it in writing.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study. If you want to withdraw your permission and not have your information shared beyond what has already been shared, please send the written notice to:

Dr. Steven R. Smith, MD
301 East Princeton Street, Orlando FL 32804
(407) 303-7100

When you withdraw your permission, no new health information that might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
If you give permission for the hospital or the investigator to share your identifiable health information to other people or businesses, the information may no longer be protected. There is a risk that your information will be released to others without your permission.

Your personal information may be disclosed if required by law. Your records for this study may be sent by facsimile transmission (FAX machine) or over the Internet. It is possible that your records could be sent to the wrong person.

How long is my information kept?
Research with private health information must be maintained for seven years after the research study has been closed at the AdventHealth Orlando site. The Sponsor may require a longer period of time.

What happens if I agree to be in research, but later change my mind?
Participation in this study is voluntary. If you change your mind and decide that you no longer want to participate in this research study, you are free to do so at any time by informing the Principal Investigator or Study Coordinator.

Any information from the analysis/testing of biospecimens obtained before you contacted the study team will continue to be used in the research study and any remaining biospecimens will continue to be used for analysis/testing. It is important for you to know that if you choose to no longer directly participate and you want to request that your biospecimens no longer be used, that is not an option for this study.

If you decide to leave the research study, a member of the research team may follow up with you for an end of study visit.

Who can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at The Translational Research Institute for Metabolism and Diabetes (TRI-MD) 407-303-7100.

This research is being overseen by an Institutional Review Board ("IRB"). The IRB is a group of people who review and approved research studies to be conducted at AdventHealth Orlando. You may talk to them at (407) 200-2677 or FH.IRB.General@adventhealth.com if:

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

Permission to Take Part in a Human Research Study

Signature Block for Adult Participant Able to Consent

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

Printed name of participant	
Signature of participant	Date
Signature of person obtaining consent Printed Name	Date

[Use the following block if a witness will observe the consent process. E.g., short form of consent documentation or illiterate participants.]

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the participant.

Signature of witness to consent process Printed Name	Date

If signature of a witness not obtained, indicate why: (select one)

- ❑ Participant is literate
- ❑ Participant can understand and read the English language