

## Permission to Take Part in a Human Research Study



**TRANSLATIONAL RESEARCH INSTITUTE  
FOR METABOLISM AND DIABETES**

*Florida Hospital & Sanford • Burnham • Prebys*

**Title of research study:** The Influence of Glycemic Control and Obesity on Energy Balance and Metabolic Flexibility in Type 1 Diabetes.

**Investigator:** Richard Pratley, MD

**Sponsor:** Florida Hospital

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### **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:

- Are 19 to 30 years of age
- Either diagnosis of Type 1 Diabetes (for more than 1 year) or are a non-diabetic match
- Body mass index (BMI)  $\geq 18$  and  $\leq 39.9$  kg/m<sup>2</sup>
- Willing and able to comply with scheduled visits, laboratory results, and other study procedures.

### **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 Florida Hospital, you should know that your participation or lack of participation in this study will not affect your employment or relationship with Florida Hospital.

### **Why is this research being done?**

You are invited to take part in a research study because you have a diagnosis of type 1 diabetes (T1D) for at least one year or meet the criteria for a non-diabetic matching control. There has been an alarming increase in the prevalence of obesity in type 1 diabetes (T1D) in recent years. Among young adults with T1D, recent studies have shown that 31% are overweight and 15% are obese. While some of the increase in obesity in patients with T1D is likely due to historical trends in diet and physical activity affecting the general population. Another probable cause could be the widespread adoption of intensive insulin therapy for the treatment of T1D. Therefore, there is an urgent need for specific, evidence-based recommendations for the prevention and management of obesity in T1D while also aimed at optimizing glucose control and weight status. To help the development of these recommendations, this study will address energy requirements in T1D and provide information about metabolism. This will most likely lead to successful control of blood glucose and weight (Phase I). In

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In addition, this study will pilot a dietary intervention (Phase II) of a low carb, reduced calorie diet to promote weight loss and improve glycemic control for overweight T1D patients.

If you are an overweight or obese T1D and have successfully completed Phase I, you might qualify for Phase II.

### How long will the research last?

If you are enrolled into Phase I, we expect that you will be in this research study for approximately 6 weeks. If you are enrolled in both Phase I and Phase II, you will be in this research study for approximately 11 weeks.

	Visit	Day	Location/Time
Phase 1	Visit 1	Screening	TRI outpatient (2-3hours)
	Visit 2	Day 1	TRI outpatient (1-2 hours)
		Day 1-7	Phone call
	Visit 3	Day 8	Admit to TRI
		Day 9	TRI - inpatient
		Day 10	TRI - inpatient
		Day 11	Discharge Home
Phase 2	Visit 4	Day 18	TRI Outpatient (1 hour)
		Day 18-35	Phone calls
	Visit 5	Day 25	TRI Outpatient (1 hour)
		Day 25 - 31	Phone calls
	Visit 6	Day 32	TRI Outpatient (1 hour)
	Visit 7	Day 35	TRI Outpatient (1 hour)
	Visit 8	Day 37	Admit to TRI
		Day 38	TRI - inpatient
Day 39		TRI - inpatient	
Day 40		Discharge Home	

### How many people will be studied?

We expect about 33 people will take part in the entire study (24 people with T1D and 9 non-diabetic controls).

### What happens if I agree to be in this research?

This is a non-randomized, cross sectional study comparing different metabolisms of a range of body weights in individuals with and without Type 1 Diabetes. The study is designed with two phases. Everybody meeting study eligibility for the study will be enrolled in Phase I of the study. Only overweight and obese individuals with T1D will be enrolled in Phase II. If you are enrolled in Phase II, you will undergo 1 month of a low carbohydrate and reduced calorie diet. All study visits will occur at the Florida Hospital Translational Research Institute for Metabolism and Diabetes (TRI-MD). A detailed description of the visits is listed below. The study requires multiple phone calls to be completed, some of these phone calls are from a TRI- MD staff member, while others are completed by the University of North Carolina Nutrition Obesity Research Center (UNC NORC).

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

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After signing this Informed Consent Form, you will undergo an initial screening process to determine if you are eligible to participate in this study.

During each visit (except Screening Visit 1) we will review if you have had any changes in your health or medications.

**Screening Visit 1 - (Time ~2-3 hours)** This visit will occur at the TRI-MD.

- Assessment of **Medical History**, including Demographics, Medication/Supplement Use, and Health History Form
- **Physical exam:** A standard physical examination will be performed by a study physician, physician assistant, or nurse practitioner.
- **Physical Measurements.** Your **vital signs** (respiratory rate, temperature, blood pressure and heart rate), **height**, and **weight** will be measured. 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.
- **Electrocardiogram (EKG):** We will measure the electrical activity of heart your using a 12-lead electrocardiogram.
- **Blood collection.** We will collect blood while you are 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, will be drawn from an arm vein. The tests that will be performed on your blood include hematology, chemistry, HbA1c, thyroid panel, lipid panel. Repeat blood samples may be required, per provider request.
- **Urine collection:** A urine sample will be taken for a **urinalysis** and **urine toxicology screen**. If you are female and able to have children, the sample will also be used for a **urine pregnancy test**.

**Visit 2/ Day 1 - (Time ~1-2 hours)** This visit will occur at the TRI-MD

- Review of **Concomitant** medications and **adverse events**
- **Vital signs**
- **Pregnancy test** for female subjects: You will be asked to provide urine sample for pregnancy test.
- **DEXA (Dual Energy X-ray Absorptiometry)** (about **15 minutes**): This test is used to measure your body composition (fat and lean body mass). You may be asked to change into a hospital gown. For the test, you will be asked to lie on a table called a DEXA scanner. During the scan, an electronic arm will pass over your body, using low dose x-rays to record the amount of bone, fat and muscle in your body. The scan takes approximately 15 minutes and the radiation dose is less than 1 mrem, or less than half the daily radiation dose in America.
- **Continuous Glucose Monitor (CGM) placement:** If you have type 1 diabetes, you will have a CGM device placed by a member of the study staff or yourself (if you have experience with a CGM device) and will wear it for up to 7 days at a time for the duration of the study. The CGM includes a sensor, transmitter, and receiver. The sensor has a plastic body and contains a thin, small needle and sensor wire about the size of a human hair. The sensor will be placed under the skin on your abdomen. Once inserted, the needle is removed and the sensor wire remains. The transmitter is about the size of a thumbprint and snaps on top of

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the sensor. The sensor wire continuously measures the sugar level in the fluid beneath the skin every 5 minutes. The glucose information is sent by the transmitter to the receiver (a small hand-held device) using radio waves. You will also need to check your blood glucose at least every 12 hours using a home glucose monitor. A study staff member will instruct you on the use and removal of the device, as well as reinsertion of the device as needed.

- **Activity Monitor:** You will be given an activity monitor that will be worn on your waist for approximately 1 week prior to your inpatient stay. The monitor will be used to collect information about your physical activity levels and your energy expenditure levels. If you participate in Phase II of the study, you will wear the activity monitor for another 1-week period, prior to your second inpatient stay. After the monitor is worn for approximately 1 week, it will be returned to TRI-MD.

### Visits 2/Day 1-7

Two questionnaires will be completed through a phone interview done by the UNC Nutrition Obesity Research Center (UNC NORC). There will be a total of two phone calls between Visit 2 and Visit 3 (Days 1-7).

**Visit 3/ Day 8 – 11** You will be admitted to the TRI-MD Clinical Research Unit (CRU) for 4 days (3 nights).

#### Day 8- (Check-in is in evening for an overnight stay)

- Review of **Concomitant** medications and **adverse events**
- **Vital signs**
- **Activity monitor** collection
- You will be provided dinner and a possible snack

#### Day 9 (overnight stay)

- Review of **Concomitant** medications and **adverse events**
- **Vital signs**
- **Fasting blood:** We will collect blood while you are fasting; meaning no food or drink for at least 10 hours before the collection time (you may drink water and take your regular medications as scheduled).
- **FibroScan:** This ultrasound-like scan will determine the health of your liver by measuring the liver's amount of fat and stiffness. A water-based gel will be applied to your skin on the right upper abdominal area (above your liver). Slight pressure will be applied to the area and several measurements will be collected. The test takes a total of about 10 minutes, with total scan time (including setup) of approximately 30 minutes.
- **Magnetic Resonance Imaging / Elastography / Spectroscopy (MRI/MRE/MRS):** This test will investigate the health of your liver by measuring the stiffness and distribution of fat, water and other molecules. This test will also look at the distribution of fat inside of your body and the size of some 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 head phones) for the MR scans. You will lie on a table in the MR scanner on your back. A device called a 'driver' (a flat round piece of plastic attached to a tube) will be placed on the right side of your ribs

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and secured in position with a stretchy strap. This device creates a rapid ‘thumping’ used to measure your liver stiffness; the thumping will only occur during a small portion of the scanning (less than 3 total minutes). A device called a ‘coil’ (which looks like a square plastic pad) will be placed on top of the driver and your chest and abdomen. Once positioned on the table, you will be moved into the magnet. When the imaging begins, you will hear loud knocking noises and need to remain as still as possible. For several of the images you will be asked to hold your breath for up to 20 seconds. For the remainder of the images, you can breathe normally, but need to stay lying still. The table will move you in and out of the magnet slowly for different scans. You will be repositioned (asked to get off, then back on the table in a slightly different position) between some of the scans; you will have the opportunity to use the restroom if needed during those times. The entire MR procedure, including positioning on the table, preliminary guidance images, liver images and fat distribution images, will take about 1 hour and a half.

- **CMG insertion:** If you are a non-diabetic we will insert the CGM for the first time (see above under Visit 2 for further details).
- **Stool Collection:** You will be asked to provide a stool sample in a special container during your TRI visit. If you cannot produce a sample here, we will provide you with a home collection kit and instructions. You will be responsible for your collection, temporary storage, and delivery of the stool sample.
- **Questionnaires:** You will be asked to complete paper questionnaires about diet, sleep and depression will take approximately 1-2 hours.
- You will be provided with breakfast, lunch, and dinner and a possible snack.

### Day 10 (overnight stay)

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- **Whole Room Calorimeter** – 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.

**24-Hour Urine Collection:** To better understand how your body uses different foods for energy, all urine will be collected over 24 hours for during your time in the Metabolic Chambers.

**Heart Rate Monitoring:** We will place a strap on your chest, which contains a sensor

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and a Polar watch on one of your wrists during your stay in the calorimetry room to continuously monitor your heart rate for exploratory purposes.

**Activity Monitoring:** We will place a wrist and waist activity monitor for the chamber stay duration.

- You will be provided with breakfast, lunch, and dinner and a possible snack.

### Day 11

- Review of **Concomitant** medications and **adverse events**
- **Vital signs**
- Exit **calorimeter room**
- Removal of chest strap and Polar watch
- Removal of activity monitor
- Check out of TRI

### *Phase 2 (10 overweight/obese participants with T1D)*

#### Visit 3/Day 11: Initial instruction in low carbohydrate, calorie restricted diet

After exiting the calorimeter, if you are participating in Phase 2 you will meet with the research dietitian. Counseling sessions will occur weekly (days 11, 18 and 25) to review your dietary adherence and make recommendations as necessary to meet the diet prescription of a low carbohydrate, calorie restricted diet. Additional counseling can occur by phone during the scheduled twice-weekly phone calls. In-person sessions with the dietitian will include audio recording of the session. After your counseling session, you will be discharged to go home and start the low carbohydrate diet. You will continue on this diet either by foods you select (from Day 11 to Day 31) or foods we provide (starting on Day 32 through your last visit at TRI on Day 40).

**Ketone and Glucose Testing:** You will be provided with a home glucose and ketone measurement device. For the glucose testing, you will be instructed to measure your blood sugar levels at least every 12 hours. Your ketone levels should be measured at least once every day. If your ketone level is above 0.6 mmol/L, you will be asked to take some additional ketone and blood glucose measurements and contact your study site immediately for assistance with managing your diabetes. A TRI staff member will train you on how to check your blood sugar and ketone levels via a small finger stick.

#### Phone Calls (Phase 2 only)

You will be contacted by phone from a TRI-MD staff member approximately twice a week to monitor glycemic control, adjust insulin as necessary, answer any questions you may have.

**Visit 4/ Day 18 (Time ~1-2 hours)** This visit will occur at the TRI-MD.

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Home **blood glucose and ketone test** (with the provided home glucose meter)
- Urine pregnancy test

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- Diet counseling- low carbohydrate diet

### Visit 4/Day 18 - Day 24 (*phone calls*)

- At least 1 call from the TRI staff to monitor diet adherence and tolerability
- At least 2 phone calls from TRI staff member to monitor glycemic control, adjust insulin as necessary, and answer any questions you may have.
- Home **blood glucose and ketone** test to continue.
- Continue outpatient low carbohydrate diet (self-selected foods based on counseling)

### Visit 4-7/Day 18 - Day 35 (phone calls)

Two questionnaires will be completed through a phone interview done by the UNC Nutrition Obesity Research Center (UNC NORC). There will be a total of two phone calls between days 18 and 35.

### Visit 5/ Day 25 (Time ~1 hour) This visit will occur at the TRI-MD.

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Home **blood glucose and ketone test**
- Urine pregnancy test
- Diet counseling- low carbohydrate diet

### Visit 5/Day 25 - Day 31 (*phone calls*)

- At least 1 call from TRI staff member to monitor diet adherence and tolerability
- At least 2 phone calls from TRI staff member to monitor glycemic control, adjust insulin as necessary, and answer any questions you may have.
- Home glucose and ketone testing to continue.
- Continue outpatient low carbohydrate diet (self-selected foods based on counseling)

### Visit 6/ Day 32 (Time ~1 hour) This visit will occur at the TRI-MD.

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Home **blood glucose and ketone test**
- Activity monitor distribution
  
- Pick up 3-day supply of controlled diet food (low carbohydrate, 500 calorie deficit)
- Consume outpatient low carbohydrate diet for 3 days (provided foods)

### Visit 7/Day 35 (Time ~1 hour) This visit will occur at the TRI-MD.

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Urine pregnancy test
- Home **blood glucose and ketone test**
- Pick up 3-day supply of controlled diet food (low carbohydrate, 500 calorie deficit)
- Consume outpatient low carbohydrate diet (provided foods)

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**Visit 8/ Day 37-40 (inpatient):** You will be admitted to the TRI-MD Clinical Research Unit (CRU) for 4 days (3 nights).

**Day 37:** (Check-in – evening for overnight stay)

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- **Activity monitor** collection
- **Urine pregnancy test**
- Home **blood glucose and ketone test** to continue
- Inpatient low carbohydrate, 500 calorie deficit diet- dinner meal only and a possible snack.

**Day 38:** (*Overnight*)

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Inpatient low carbohydrate, 500 calorie deficit diet- controlled meals three times a day and a possible snack.
- **Fasting blood samples** will be collected
- **Magnetic Resonance Imaging / Elastography/ Spectroscopy (MRI/MRE/MRS)**
- **Stool collection** and banking
- Paper **questionnaires**
- Home **blood glucose and ketone test** to continue

**Day 39:** (*Overnight*)

- Review of **concomitant** medications and **adverse events**
- **Vital signs**
- Inpatient low carbohydrate, 500 calorie deficit diet- controlled meal three times a day and a possible snack.
- Check into **whole room calorimeter** for 23 hours
- Placement of continuous heart rate monitor (chest strap and Polar watch)
- Placement of activity monitor on wrist and waist
- 24-hour urine collection
- Home **blood glucose and ketone test** to continue

**Day 40:**

- Review of **Concomitant** medications and **adverse events**
- **Vital signs**
- Inpatient low carbohydrate, 500 calorie deficit diet - breakfast only
- Check out of **whole room calorimeter**
- CGM collection
- Removal of chest strap and Polar watch
- Removal of activity monitor
- **Blood glucose and ketone test** done at TRI
- Check out of CRU and resume your usual diet

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

Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study. If you take part in this research, you will be responsible to tell your study doctor about all of your past and present health conditions, including allergies of which you are aware, and all drugs and medications you are presently using.

### ***What other choices do I have beside taking part in the research?***

Instead of being in this research study, your choices may include not participating. You may want to consider discussing additional treatment options with your primary care physician.

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

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.

**Intravenous (IV) Line and blood draws (lab samples, e.g.)** – You will undergo needle sticks during visits where blood samples are collected or IV catheters are placed. You may have pain, light-headedness, infection, fainting, bruising, bleeding, and/or clotting at the site of needle insertion. There is a possibility that a catheter placement would be unsuccessful or need to be removed. If this should occur, another catheter would be placed. It is possible that this may occur more than once during your participation in the study. However, the staff will use proper technique while taking blood samples and managing IVs 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 for research purposes will be approximately 0.3 cups (65ml), over a period of about 18 months. In comparison, the typical amount collected during a blood bank donation is one pint (2.25 cups/540ml). ***It may be necessary to repeat lab work for safety or verification of results based on the assessment of the study providers or sponsor.***

After certain blood collections, a small amount of your own blood (less than 1 tsp) may immediately be returned into your vein through the IV line.

**Vital Signs/ Blood Pressure testing:** You may experience temporary discomfort during blood pressure recording due to the pressure of the cuff on the arm.

**Waist/Hip:** Measurement of the waist and hip circumferences is non-invasive and not associated with any risks.

**Stool collection:** There are no known risks with collecting and storing stool.

**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, less than half the amount you receive each day, or less than a chest X-ray. During the study, you will receive one DEXA scan which is equivalent to less than the average daily radiation dose in America. 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.

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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.

**Magnetic Resonance (MRI/MRE/MRS):** There are no known biological risks associated with magnetic resonance imaging and spectroscopy. Some short-term discomfort may be experienced. The short-term risks associated with MRS are minimal, but include a feeling of warmth, loud noises and claustrophobia. There is a small risk of skin irritation at the site of the electrodes after the removal of the sticker. If this occurs, it is usually mild and goes away within a day or two. There are some people who should not undergo MRI; 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.

**Fibroscan:** There are no known risks associated with FibroScan®.

**Continuous Glucose Monitoring (CGM)** During Visit 2 (if you are a type 1 diabetic) and Visit 3 (for non-diabetic) you will have the initial insertion of a continuous glucose monitor and you will wear it for the duration of the study. The CGM will be placed by a member of the study team who will instruct you on how to care for it at home. The CGM that you will be provided is approved by the Food and Drug Administration (FDA). The CGM kit has a sensor, transmitter and receiver. The sensor has a plastic body and contains a thin, small needle and sensor wire about the size of a human hair. The sensor will be placed under the skin on your belly. Once inserted, the needle is removed and the sensor wire remains. The transmitter is about the size of a thumbprint and snaps on top of the sensor. Special tape is used to keep the sensor in place. The sensor wire continuously measures the sugar level in the fluid beneath the skin every 5 minutes. The glucose information is sent by the transmitter to the receiver using radio waves. The receiver is the small hand-held device that looks like a MP3 player. The receiver will be connected to a computer to retrieve the blood sugar readings.

The CGM will not be blinded which means the sugar levels will be visible to you. To ensure the CGM works properly, a clinical staff member will either check or ask you to check your blood glucose levels at least every 12 hours (twice a day) with a glucose meter.

The risks of wearing the CGM are minimal. Bruising, redness, discomfort, and some bleeding can occur. Mild skin irritation is common, rarely an infection can occur at the side of the CGM sensor needle placement. An allergic reaction to the tape used to hold the sensor in place is possible. If there is pain, redness, irritation, or rash at insertion site, the sensor will be removed and re-inserted in a different site.

**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.

**Activity Monitor:** There are no risks associated with the wearing of activity monitors. However, the band that holds the monitor in place may be irritating to the skin for some subjects. Participants with nickel allergies may have irritation at the site of the monitor.

**Heart Rate Monitor (chest strap and Polar watch):** There are no risks associated with the wearing the heart rate chest strap and/or the Polar Watch.

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

**Study Diet:** With a change in diet it is possible that subjects will experience gastrointestinal (GI) symptoms on one of the diets such as flatulence, cramping, diarrhea, or constipation. There are also risk due to the low carb diet and changes in insulin dosing that you might experience hypoglycemia (low blood sugar levels), hyperglycemia (high blood sugar) and possible diabetic ketoacidosis (increase in ketones in the blood and urine).

**Blood glucose and ketone** testing will be done by finger stick with a small blood sample, which could cause some mild discomfort, pain bruising and a small risk of infection.

**Low and/or High Blood Sugar:** If you experience any signs or symptoms of hypoglycemia (low blood sugar) or hyperglycemia (high blood sugar) you should take your blood sugar reading and contact your study doctor.

- Hypoglycemia (low blood sugar) signs and symptoms may include but are not limited to: fast heartbeat, shakiness, nervousness or anxiety, sweating, hunger, nausea, headache, weakness, dizziness, lightheadedness, tingling around the mouth, disorientation, confusion, slurred speech, abnormal behavior, double or blurred vision, seizure, loss of consciousness.
- Hyperglycemia (high blood sugar) signs and symptoms may include but are not limited to: headache, dry mouth, thirst, frequent urination, blurred vision, dry itchy skin, fatigue, drowsiness, confusion, difficulty breathing, dizziness upon standing, rapid weight loss, confusion, loss of consciousness.

**Diabetic Ketoacidosis (DKA)** is a serious condition which occurs in some people with diabetes which causes ketones to build up in the blood and appear in the urine. The following list of symptoms may help you to recognize Diabetic Ketoacidosis (DKA):

- Difficulty breathing
- Inability to maintain oral intake (cannot eat or drink)
- Generalized weakness
- Abdominal (belly) pain
- Increased weight loss
- Fever
- Frequent urination, including at night
- Fruity-scented breath
- Confusion or having trouble thinking clearly
- Feeling acutely ill
- Feeling very thirsty or drinking a lot
- Nausea (feeling sick to your stomach) or vomiting
- Feeling very tired

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If you have any of these symptoms on the list, you will be asked to measure your blood ketones more than once a day, using a home device, that has been provided as part of the study.

You will be provided instructions on how to recognize hypoglycemia (low blood sugar), hyperglycemia (high blood sugar) and diabetic ketoacidosis. If you have any hypoglycemic, hyperglycemic symptoms, or your ketone levels that are greater than 0.6mmol/L or if you have any of the above DKA symptoms, please contact your study doctor immediately at:

Translational Research Institute for Metabolism and Diabetes  
301 E Princeton Street  
Orlando, FL 32804  
407-303-7100

**Incidental 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.

**Pregnancy:** 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.

**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.

### ***Will being in this study help me in any way?***

There are no benefits to you from taking part in this research. No promises can be made concerning the study outcome, because results from a clinical research study cannot be predicted. Your participation may help researchers obtain additional information on the predictors of health in the general population. Your alternative is to not take part in this research study.

### ***Are there any costs in this study?***

The TRI-MD will provide all the supplies and procedures that are specifically related to the study free of charge during this study. Tests and procedures that are done only for the study will not be billed to you or your insurance company. All standard of care procedures and medical needs related to medical conditions will be billed to you or your insurance company.

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.

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*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 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 to a treatment.

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

Dr. Richard Pratley  
Florida Hospital Translational Research Institute for Metabolism and Diabetes  
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 must review it. We cannot promise complete secrecy. The 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.

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 Florida Hospital. If this is needed, provisions will be put in place to protect the confidentiality of your information.

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.

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

## **Permission to Take Part in a Human Research Study**

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 Florida Hospital 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 limit the use of your samples specifically for research that is similar to the purpose/aims of this research study and that it has scientific merit.

Some information will be provided to the University of North Carolina (UNC), such as name, phone number, and best times to contact you. The information will be stored in a secure online database developed and maintained by the UNC Cecil Sheps Center for Health Services Research. Access to the information is only accessible via specific login and is only available to approved study site staff and trained UNC interviewers. All data entered in the NDSR data analysis system is deidentified and a study ID is used in place of any identifying information to enter data. There is no link from participant ID to sensitive participant information. Once all data collection is complete, all participant and related study information is permanently deleted from the UNC Sheps database.

### ***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 do not follow study instructions;
- TRI-MD stopping the study
- Administrative reasons

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?***

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.

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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.

This research is being funded by the University of North Carolina (UNC) through NIDDK and Florida Hospital.

If you agree to take part in this research study, we will pay you up to a total of \$660 (Phase 1) and a total of \$1,495 (Phase 1 and Phase 2 combined) for your time and effort. You will only be paid for completed visits. If you withdraw from the study prior to completing all procedures, your payment will be prorated for completed visits according to the information below. The compensation check may take approximately 2 weeks to be processed once requested. You will be paid at the completion of each Phase.

Phase 1		Phase 2	
Visit 1 (Screening)	\$ 50	Visit 4	\$ 75
Visit 2 (Day 1)	\$ 75	Visit 5	\$ 75
Visit 3 (Day 8)	\$ 125	Visit 6	\$ 75
Visit 3 (Day 9)	\$ 125	Visit 7	\$ 75
Visit 3 (Day 10)	\$ 200	Visit 8 (Day 37)	\$ 125
Visit 3 (Day 11)	\$ 85	Visit 8 (Day 38)	\$ 125
<b>Total Phase 1</b>	<b>\$ 660</b>	Visit 8 (Day 39)	\$ 200
		Visit 8 (Day 40)	\$ 85
		<b>Total Phase 2</b>	<b>\$ 835</b>

### ***HIPAA Authorization to Release Information for Research***

If you have not received a copy of the Florida Hospital Privacy Notice, please request one. If you have questions about your privacy rights, you may contact Florida Hospital'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, Florida Hospital personnel, and individuals who provide health care services at Florida Hospital to disclose

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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
- Date of Birth
- Other details about you
- 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.*)

### 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. This study also includes a number of researchers at University of North Carolina at Chapel Hill and Stanford University and government agencies who will receive your data.

### Who may see this information?

The study sponsor may see your health information and know your identity. “Sponsor” includes people 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
- Florida Hospital representatives
- Institutional Review Board (IRB)
- Accreditation organizations
- Publications, medical meetings, or scientific journals (individual patients will not be identified).
- University of North Carolina at Chapel Hill
- Stanford University

### 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

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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 Florida Hospital 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. Richard Pratley, MD Address:**  
**301 East Princeton Street, Orlando FL 32804**  
**Phone Number: 407-303-7100**  
**or**  
**Research Study Coordinator Address:**  
**301 East Princeton Street, Orlando FL 32804**  
**Phone Number: 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.

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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 Florida Hospital site.

### ***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.

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. Any analysis/testing that was already performed or that is in progress at the time of your request to withdraw from this research study will continue to be used as part of the research study. Should you decide that you do not want any of your remaining biospecimens to be stored for additional analysis/testing, you may contact the Principal Investigator listed on the front page of this form to tell him/her that you no longer wish to have your biospecimens stored. After you notify the Principal Investigator, your remaining biospecimens will not be used and will be destroyed.

If you end your study participant before the final regularly scheduled visit, you may be asked by the study doctor to make a final visit for end of study follow-up to ensure there are no safety concerns.

If you stop being in the research, already collected data may not be removed from the study database.

### ***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

**Dr. Richard Pratley, MD**  
**Address: 301 East Princeton Street, Orlando FL 32804**  
**Phone Number: 407-303-7100**

or

**Research Study Coordinator**  
**Address: 301 East Princeton Street, Orlando FL 32804**  
**Phone Number: 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 Florida Hospital. You may talk to them at (407) 303-5581 or [FH.IRB.General@flhosp.org](mailto:FH.IRB.General@flhosp.org) 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 subject.
- You want to get information or provide input about this research.

## Permission to Take Part in a Human Research Study

### Signature Block for Adult Subject Able to Consent

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

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Printed name of subject

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Signature of subject

---

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 subjects.]***

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 subject, and that consent was freely given by the subject.

---

Signature of witness to consent process

---

Printed Name

---

Date

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

- Subject is literate
- Subject can understand and read the English language