IRB Protocol #2000029479
NCT04955691

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Metabolic and Neurological Changes Induced by a Very Low Carbohydrate Diet in Youth with Type 1 Diabetes

Principal Investigator (the person who is responsible for this research):
Laura Nally, MD
One Long Wharf Drive, Suite 503
New Haven, CT 06511
Phone Number: **203-785-5831**
24-Hour Phone Number: **203-785-5831**

In the following document, "you" can also refer to "your child".

Research Study Summary:

- We are asking you to join a research study.
- The study will look at how your blood sugar and metabolism changes when you are on a standard carbohydrate diet when compared to a low carbohydrate diet.
- Study procedures will include wearing a continuous glucose monitor (CGM), wearing an activity monitor, following a very low carbohydrate diet, measuring daily blood ketone levels, keeping a food journal, talking to research staff 2-3 times per week, sharing your CGM data and insulin pump information.
- **Six** visits are required over 8-12 weeks
- These visits will take **1-16** hours total.
    - Visit 1 will be an enrollment visit that lasts ~1 hour.
    - Visit 2 will be an in person or telephone/virtual visit and will last about 30 minutes.
    - Visit 3 will take place at the
        - Hospital Research Unit (HRU) and will last 16 hours, or
        - Masonicare and will last 16 hours, or
        - Church Street Research Unit (CSRU) and last ~8 hours.
    - Visit 4 will be an in person or telephone/virtual visit and will last about 30 minutes
    - Visit 5 will take place at the
        - Hospital Research Unit (HRU) and will last 16 hours, or
        - Masonicare and will last 16 hours, or
        - Church Street Research Unit (CSRU) and last ~8 hours.
    - Visit 6 will take place over the phone or via Zoom and last 20-30 minutes.
- There are some risks from participating in this study. **Every research study includes the risk of loss of privacy. There is also a risk of high or low blood sugars when changing diets during the study. The infusion study will cause hypoglycemia for a short period of time. There is the risk of anemia due to the blood draws that take place during the study.**
- The study might benefit you by improving your blood sugars by reducing low blood sugars and reducing high blood sugars. You may also learn more about how nutrition can affect your blood sugars. The study might help other people by helping scientists understand more about how low carbohydrate diets affect blood sugars, the production of ketones, and hypoglycemia symptoms. This study will also help inform clinicians taking care of patients to ensure they understand the risks and benefits of this diet.

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- There are other choices available to you outside of this research. Get treatment without being in a study. You can follow a very low carbohydrate diet without participating in the study, however we do not know the long-term risks and benefits of following this diet. You may also take part in another study.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?

We are asking you to take part in a research study because **you have type 1 diabetes**. We are looking for **20** participants to be part of this research study.

Who is paying for the study?

The Diabetes Research Center at Yale and National Institutes of Health have provided grants to pay for this study.

Who is providing other support for the study?

No other organizations are providing support for this study.

What is the study about?

The purpose of this study is to see how a very low carbohydrate diet can help you manage your blood sugars and see how hormone levels and metabolism changes as a result of the diet. We also want to see if your response to hypoglycemia (low blood sugar) changes on a very low carbohydrate diet.

What are you asking me to do and how long will it take?

If you agree to take part in this study, this is what will happen:

Visit 1: Enrollment (1 hour)

- A handout with 2 examples of the type of diet required will be provided to you prior to consent. We will review this consent form prior to any study activities.
- We will ask you questions about your diabetes management, past medical history, social history, and other information about you. If you have an insulin pump or CGM, we will collect that information as well.
- We will measure your height, weight, and percent body fat, muscle, water, and bone using a special scale, and will perform a physical exam. The study doctor may also look for changes that take place at puberty.
- We will measure a Hemoglobin A1c level if one has not been checked in the past 2 months.
- We will ask you to provide us with a 3-day diet history.
- You will fill out 3 questionnaires that ask you about your diabetes management, nutritional knowledge, and stressors related to diabetes.
- We will provide you with a blood ketone meter and show you how to use it. You may keep the blood ketone meter.

- If you do not already have a CGM, we will provide you with one and show you how to use it. You may keep the CGM.
- We will provide you with an activity monitor and a scale. We will also help you download an app to collect this information.
- We will schedule telephone follow up calls. After you go home, our research staff will call you 1-2 times per week to review your diet, your blood sugars, and insulin doses for the next 1-3 weeks.
- You will be given instructions on how to upload your continuous glucose monitor and insulin pump using Tidepool.

Visit 2 Randomization & Visit 4 (in person or virtual/telephone, 30-45 minutes)

- We will randomly decide (like flipping a coin) which diet you will start.
- We will give you instructions the first study diet (may be a standard carbohydrate or a very low carbohydrate diet).
- Standard diet: We will give you instructions on how to follow a standard carbohydrate diet of at least 150 grams of carbohydrates per day (or at least 30% of your total daily caloric intake). We will ask you to keep a diet journal of everything that you eat (My Fitness Pal, photos, written journal) for the 14 days of the standard carbohydrate diet. You will check daily fasting ketone levels to ensure your ketones remain below 0.3 mmol/L and may ask you to eat more carbohydrates each day if your ketones remain above this level. Research staff will schedule calls on 2 days each week to perform a 24 hour dietary recall and we will call you 1 additional day for a 24 hour dietary recall without giving you advanced notice. You will need to turn in the full 14-day journal at the follow up visit.
- Very low carbohydrate diet: We will give you instructions on how to pick up food from the metabolic kitchen (or food delivery service if the metabolic kitchen is unavailable) for the very low carbohydrate diet portion of the study. We will provide you with 3 meals daily for 14 days. We will ask you to only eat 50-75 grams of carbohydrates daily. However, the dietary requirements may change to some degree based on your blood sugar and ketone levels. We will ask you to check daily fasting ketone levels. You will not be allowed to drink alcohol during this portion of the study. The goal of the diet is to allow you to make a small amount of ketones (at least 0.3 mmol/L) each day, and the diet will be adjusted to help you meet this goal. We will give you a checklist with each of the meals and ask you to circle each meal that you eat (and the date) and write in any additional snacks that you have. Research staff will schedule calls on 2 days each week to perform a 24-hour dietary recall and we will call you 1 additional day for a 24-hour dietary recall without giving you advanced notice. You will need to return the full 14-day journal at the follow up visit.

Visit 3 & Visit 5 (HRU/CSRU/Masonicare Visits, overnight visit or outpatient):

- Prior to the infusion, we recommend that you avoid strenuous exercise 3 days before these tests. This will help us collect more reliable information from the tests.
- For the outpatient study, you will be asked to come in the day before the infusion study to have blood tests done and will be provided with a special type of water and instructed on when to drink it overnight. You will return the following morning at 7am to complete the infusion study.
- We will also have you drink a special type of water (deuterated water), a naturally occurring compound. This will allow us to track the origin of sugar made by the liver. The amount of deuterated water given depends on body weight and body water. For participants <154 lbs, the volume of deuterated water will be less than 1 cup, divided up

into 3 doses. For participants 154 lbs. or more, the volume of deuterated water will be slightly more. This will be provided prior to the visit for the infusion study with instructions on when to drink it. The night before the test, we recommend that you have a snack at 9pm, but you should not eat any food or drink liquids other than water after 12am. You will not eat breakfast the morning of to the Infusion Study.

- If you will be doing the overnight study, we will ask you to come in at 6pm on the evening prior to the infusion study. We perform blood tests and will provide the deuterated water for you to drink overnight.

Infusion Study:

- You will be asked to come to either the Hospital Research Unit (an area of the hospital where research studies are conducted) or Church Street Research Unit. The study nurse will do a nursing assessment, including measuring your height, weight, temperature, blood pressure, and pulse. The nurse may also obtain a family and medical history. If you are female, a urine pregnancy test may be performed. A television and VCR will be available for you to watch during these studies.
- We will have your complete questionnaires at this visit. These questionnaires will ask questions about how diabetes makes you feel, what causes you stress about your diabetes, and your satisfaction with your current diabetes management (and diet).
- To give insulin and to prepare you for the study, two small I.V.'s (small plastic tubes) will be placed in a vein in each arm. If you prefer, a numbing cream (Emla) can be used prior to the IV placement.
- Your insulin pump will be suspended but you may continue to wear your CGM. During the first 2.5 hours, you will receive insulin to keep your blood sugar stable through an I.V. that will give you insulin, glucose, and glycerol solutions. A second I.V. will be used to take out small amounts of blood for measuring glucose and other substances that circulate in the blood. This I.V. will be used to obtain blood samples to measure hormones and other metabolic testing (glucagon, c-peptide, free fatty acids, ketone levels).
- For the overnight study, the infusion will begin between 5-6 am. For the outpatient study, it will begin at 7:30 am.
- We will start the infusion of glucose and glycerol solutions labeled with a stable isotope (a nonradioactive, naturally occurring atom). This will not be enough glucose to affect your blood sugar levels in a harmful way. It will allow us to measure the release of glucose from the liver and glycerol from fat tissue. The insulin infusion will continue and will be adjusted to keep your blood sugars stable (90-110 mg/dL).
- During the first part of the study (2.5 hours), measures of glucose and glycerol will be collected through the I.V. line every 10 - 30 minutes. Additional blood tests will be done to look at your metabolism (insulin, free fatty acid, and glucagon levels).
- During the second part of the study (90 minutes), the amount of insulin you are given will be increased and dextrose will be given to keep your blood sugars stable (between 90-95 mg/dL). This part of the study will test how sensitive your liver is to insulin. Blood sugar readings will be taken every 5 minutes.
- During the third part of the study (120 minutes), the amount of insulin you are given will be increased to a higher amount and the dextrose will also be increased to keep your blood sugars stable (between 90-95 mg/dL). This part of the study will test how sensitive your skeletal muscle is to insulin. Blood sugar readings will be taken ever 5 minutes.
- Up to 3 times during the infusion study, we will ask you to wear a plastic hood (like an astronaut space helmet) for about 30 minutes, this is called Indirect Calorimetry. These measurements will allow us to calculate how much glucose and fat your body is burning.

- If you need to urinate during the infusion study, you will be allowed to use a bedpan or get up to use the bathroom if necessary.
- During the fourth part of the study, we will reduce the dextrose and insulin concentrations and allow your blood sugars to naturally fall to ~55mg/dL where we will keep them for 60 minutes. Blood sugars will be monitored every 5 minutes and dextrose can be adjusted to maintain this level and prevent severe hypoglycemia. During this time, we will measure hormones that help raise your blood sugar, including glucagon, epinephrine, norepinephrine, and cortisol during this time. After 20-25 minutes at 55mg/dL, we will ask you questions about what symptoms you are feeling related to hypoglycemia.
- Once the infusion study is complete, the insulin infusion will be stopped and the dextrose infusion will be adjusted to help your blood sugars return to at least 80 mg/dL.
- The nurse will make sure your blood glucose is at the proper level before removing the I.V.s. Once the infusion study is completed you will be served lunch. The duration of this test is about 8 hours and should finish at approximately 4 pm (outpatient study) or 2:30pm (overnight study).

Washout Period: After visit 3 and before visit 4, you will resume your usual diet for the next 1-3 weeks. We will schedule telephone follow up calls. After you go home, our research staff will call you 1-2 times per week to review your diet, your blood sugars, and insulin doses for the next 1-3 weeks.

Visit 6: You will meet with a study team member over the phone or over Zoom which will be recorded. The study team member will ask you some questions about how you felt following the low carbohydrate diet, and what you liked and disliked about the diet. Answers to these questions will be kept confidential. The interviews will take 20-30 minutes.

What are the risks and discomforts of participating?

Risk of Loss of Privacy: In order to protect your privacy, the HIPAA-trained personnel will assign you a study code. Identifiers will be protected—assent forms and study files will be kept in a locked file cabinet. Your name and date of birth will be kept in a password-protected computer database, located in a locked file on a secure server with access restricted to study investigators. The Yale regulatory committee will be able to review study records but scientific publications will refer to the subjects by study identifiers only.

Risks of Infusion Study:

- This study involves the placement of an I.V. in a vein in your hand or arm, which can cause a bruise or discomfort. Rarely, infection, a blood clot, inflammation, or bleeding can occur at the site.
- If pain is a concern, we can use a special numbing medicine that will minimize the pain. You may be given Tylenol if needed.
- If inflammation of the vein (also called phlebitis) occurs, application of a warm soak to the site and elevation of the arm will help.
- Very rarely, a person may faint, or more likely become lightheaded or nauseated, when the I.V. is placed.
- Although also very rare, it is possible that you may feel nauseated, get a headache, or feel shaky or lightheaded during or after the studies involving the I.V.
- All I.V.s will be placed and removed while you are sitting or lying in bed in case dizziness occurs. In addition, the nurse will make sure your blood glucose is at the proper level before

removing the I.V.s. The nurses who put in the I.V.s have special training and experience in drawing blood and in working with adults, children, and adolescents. This should help keep the risks at the very lowest level possible.

- Your blood glucose will be watched very closely (every 5-15 minutes) throughout the infusion studies to ensure that it does not fall too low or rise too high.
- Your blood pressure and heart rate will be checked at the beginning of the infusion studies to ensure you are stable. The nurse will then assess you throughout the study.
- The infusion study includes use of stable isotopes. Despite the theoretical risk of infection with infusion of stable isotopes, our team has been using isotopes during clamp studies for over 15 years in children, adolescents, and adults and have not experienced any adverse events. Isotopes will be carefully monitored and administered, and will be prepared in the investigational pharmacy to ensure proper technique is used.
- The risk of using deuterated water during the diet study appears to be negligible. This compound will be given orally, therefore there will not be any risk related to sterility and infections. This special water that you will drink has no known risks, and it has been given to younger children for clinical purposes with no negative effect.
- The total amount of blood that will be collected for the study is 15 tablespoons (~221 mL or a little less than 1 cup) and should not present any significant problem. You should not donate blood or have a large volume of blood taken for any purpose outside of this study for two months following each study that takes place at the CSRU.

Risks of Indirect Calorimetry (wearing a hood): Although rare, during the Indirect Calorimetry portion of the study, you may feel nauseated and/or claustrophobic (anxious over being in an enclosed place) while wearing the plastic hood. In addition, the air under the hood may become warm and stuffy, which some people find uncomfortable. You can request to remove the hood if you are uncomfortable, and it will be removed.

Risks of hypoglycemia or hyperglycemia (clamps): During this study, we will give you insulin through an I.V. and adjust the dextrose concentration to keep your blood sugars between ~90-110 for the majority of the time during the visits to the HRU/CSRU/Masonicare. During the last 60 minutes of the visit, we will allow your blood sugars to drop to 55 mg/dL, and we will keep them at that level for 60 minutes. We will be closely monitoring venous blood sugar levels every 5 minutes and can give dextrose or reduce insulin to allow blood sugars to return to normal at any point if requested by the participant. Close monitoring of venous glucose levels ensures that there will be minimal risk that the blood sugar levels will become dangerously low. Further, because of the close monitoring and ability to give insulin through the I.V., it is unlikely that severe hyperglycemia or ketosis will occur.

Risks of very low carbohydrate diet: A low carbohydrate diet can cause symptoms, including headaches, nausea, vomiting, abdominal pain, constipation, fatigue, and lightheadedness. You will be asked about these symptoms at follow up visits. It is important to stay well-hydrated and eat enough calories each day to avoid these symptoms. You will develop a low level of ketones during the low carbohydrate diet portion of the study. You will check your ketone levels each morning and any time you have nausea, vomiting, headache, or symptoms of high ketone levels just like you would normally do. If ketone levels are elevated too much, you should call our on call doctors and they can help you manage them.

Risks of study questionnaires/interviews: Participants may experience stress when discussing factors that affect diabetes management because it is a sensitive topic for many people.

Risks of CGM use: There is a low risk of developing a local skin infection at the site of the sensor needle placement. Itchiness, redness, mild bleeding, and or bruising may occur at the insertion site. Subjects may develop localized reactions to adhesive used to secure the sensor.

Risks of activity monitor: There is a low risk that the fitness wrist smartwatch will contribute to skin irritation or allergies. We will show you how to keep the device dry, not wear it too tightly, and remove it for an hour every couple of days.

Pregnancy testing: Female subjects of childbearing potential will require urine pregnancy testing prior to proceeding with the protocol. Pregnancy tests will be performed at visits 3 and 5 prior to the clamp procedures. If you are 13 or older, only you will be told the results. We will, of course, counsel you to seek appropriate healthcare and the support of an adult if you were found to be pregnant. A positive pregnancy test means that you cannot participate in this study. Because you will be asked to leave the study, your parents may find out that you are pregnant. If you or your parent is uncomfortable with pregnancy testing, then we would recommend that you do not participate in the study. Methods of contraception (birth control pills, condoms, etc.) must be used for the entire duration of the study.

How will I know about new risks or important information about the study?
We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?
The study might benefit you by improving your blood sugars by reducing low blood sugars and reducing high blood sugars. You may also learn more about how nutrition can affect your blood sugars.

How can the study possibly benefit other people?
The study might help other people by helping us understand more about how low carbohydrate diets affect blood sugars, the production of ketones, and hypoglycemia symptoms. This study will also help inform clinicians taking care of patients to ensure they understand the risks and benefits of this diet.

Are there any costs to participation?
If you take part in this study, you will not have to pay for any services, supplies, study procedures, or care that are provided for this research only (they are NOT part of your routine medical care). However, there may be additional costs to you. These can include costs of transportation and your time to come to the study visits. YNHH parking garage validation will be provided overnight stays (visit 3 and visit 5) You or your health insurance must pay for services, supplies, procedures, and care that are part of your routine medical care. You will be responsible for any co-payments required by your insurance.

Will I be paid for participation?
You will be paid for taking part in this study. You will receive $10 for Visits 1, 2, and 4. You will receive $120 for Visits 3 and 5, $50 per 2-week diet record that is completed at least 70% or 5/7 days per week and $20 for completing the Visit 6 interview. You will also receive $30 for wearing the CGM at least 85% of the time. The maximum total compensation you can receive is $420 for completing all parts of the study. You will receive compensation for whatever parts of the study you complete**.** We will use a pre-paid debit card to provide the stipend for taking part in the study. We will have to share

your name, address, and telephone number with the banking institution issuing the debit card for ePayments. You will receive a card in the mail. You will need to activate the card over the phone. Each additional payment will be automatically added to your card. You may be responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you have some other choices.
You could:

- Get treatment without being in a study. You can follow a very low carbohydrate diet without participating in the study, however we do not know the long-term risks and benefits of following this diet.
- Take part in another study.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

Information about you will be kept in a locked research office that requires badge access, and any electronic forms will be maintained on a computer that requires a password for authorized users. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific permission is obtained.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

Identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility.
We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects. The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institute of Diabetes and Digestive and Kidney Diseases, which

is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of as child abuse and neglect or harm to self or others. The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, such as including research data in the medical record.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called "Protected Health Information." It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this Study.
- The entire research record and any medical records held by ***Yale New Haven Hospital*** created from: ***1/1/2010*** to ***the end of the study.***
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Other reportable infectious diseases
    - Physical exams
    - Laboratory, x-ray, and other test results
    - Diaries and questionnaires
    - The diagnosis and treatment of a mental health condition
    - Use of illegal drugs or the study of illegal behavior
    - Records about any study medications you received
    - Records about any devices you used during the study
    - Interview Recordings

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about ***continuous glucose monitor or insulin*** involved in this research. The

information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor or manufacturer of study drug/device
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Principal Investigator of the study
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to the principal investigator at the Yale University.

Laura Nally, MD
One Long Wharf Drive, Suite 503
New Haven, CT 06511

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. If you have more than 1 episode of severe hypoglycemia during the study, you will be removed from the study for your safety. If you are not able to wear your continuous glucose monitor at least 75% of the time, follow the study diet, and follow study procedures, you will not be able to continue to participate in the study.

What will happen with my data if I stop participating?

If you decide to withdraw from the study, any data that has been collected will be de-identified but will still be analyzed and reported as a part of the study.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at **203-785-5831**

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

APPROVED BY THE YALE UNIVERSITY IRB 10/12/2023

Complete if the participant is not fluent in English and an interpreter was used to obtain consent. Participants who do not read or understand English must not sign this full consent form, but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only. If the interpreter is affiliated with the study team, the signature of an impartial witness is also required.

Print name of interpreter: _____

Signature of interpreter: _____ Date: _____

An oral translation of this document was administered to the participant in _____ (state language) by an individual proficient in English and _____ (state language).

Print name of impartial witness: _____

Signature of impartial witness: _____Date: _____

See the attached short form for documentation.