Consent Form (includes HIPAA Authorization)

Title of Research Study: Prolonged Daily Fasting as a Viable Alternative to Caloric Restriction in At-Risk Obese Humans **(See Food Study 2)**

Investigator Team Contact Information:

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Investigator Name : Lisa Chow, MD **Investigator Departmental Affiliation:** Department of Medicine- Division of Endocrinology, Diabetes and Metabolism **Phone Number:** 612-625-8934 **Email Address:** chow0007@umn.edu	**Study Staff:** Alison Alvear, PA **Phone Number:** 612-624-3588 Abdisa Taddesse **Phone Number:** 612-624-1469
	Stephanie Singroy **Phone Number:** 612-301-7130
	Email Address: endores@umn.edu

Your doctor, who is also responsible for this research study, is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Supported By: ***This research is supported by National Institute of Health (NIH).***

Key Information About This Research Study

The following is a short summary to help you decide whether or not to be a part of this research study. More detailed information is listed later on in this form.

What is research?

Doctors and investigators are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Investigators learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.
- The goal of clinical care is to help you get better or to improve your quality of life. Doctors can make changes to your clinical care plan as needed.

Research and clinical care are often combined. One purpose of this informed consent document is to provide you clear information about the specific research activities of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you are between the ages of 18 and 65 and are overweight or obese.

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.

Why is this research being done?

The purpose of the study is to see whether restricting your eating window (called time-restricted eating) or reducing your food intake might affect your eating habits, weight, body composition and blood measures more than just watching what you eat every day. Time-restricted eating means that you would limit your eating window over the course of a day to within an 8 hour time period.

How long will the research last?

We expect that you will be in this research study for about 16 weeks. The research surveys will take up to six additional months to complete.

What will I need to do to participate?

You will be assigned to one of three groups, Time-restricted eating (TRE), Caloric Restriction (CR), and Unrestricted Eating (non-TRE), be asked to complete 6 phone visits 5 in person visits at the University of Minnesota, and 2 virtual visits. Visits 3 and 6 will last about 8 hours; a glucose clamp will be performed during those visits.

You will be asked to have blood draws and provide urine samples at different study visits, fill out questionnaires about your lifestyle, we will take height and weight, ask you to download "My Circadian Clock" mCC app, a free app, onto your smart phone, wear a sensor to monitor your activity and sleep (for about 2 weeks at the beginning and end of the study), have a glucose sensor placed on your skin during Visit 1 and Visit 5, which involves inserting a small tube, called a catheter, into the skin (for about 2 weeks and then removed), complete a DEXA Scan (which is a type of x-ray that measures your bone mineral density and bone loss), complete an MRI (which is a scan that takes pictures of your body), and you will be provided a meal to eat at home the night before study visits 3 and 6 (the study team will provide you the meal) . You will need to fast after those meals (water and medications are allowed) for the next day.

<u>While on this study, you will be asked to fast. Some of your current medications may direct you to take food with your medication. Ideally, you would move the timing of the medication to correspond with the window. However, if this unable to be done, you may take the medication with food as scheduled. Even if the timing of the medication is outside your fasting window. If you have any questions/concerns about when you should take your medications please ask the study staff or your provider.</u>

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

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

Time-restricted Eating:

If you are assigned to the time-restricted eating group, you may feel hungry outside of the window in which you are allowed to eat.

Fasting:

While fasting in this study you could feel hunger and lightheadedness. You will be asked to drink water to keep yourself hydrated. The fasting period will be less than 24 hours.

Questionnaires:

The questions asked of you in this study relates to your eating habits, perception of food and hunger, and quality of life. It is highly unlikely that the questions that are asked of you in this study may make you feel uncomfortable. That being said, some of the questions asked may be potentially sensitive in nature and may be embarrassing for some people to answer. You do not have to answer any questions that you do not want to answer.

More detailed information about the risks of this study can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)" and in the "What happens to the information collected for the research?" section.***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. We do not know if restricting the eating window is different than caloric restriction versus watching your food intake. Information learned in this study will help us provide dietary advice to future patients.

What happens if I do not want to be in this research?

There are no known alternatives, other than deciding not to participate in this research study.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 250 people here will be in this research study.

What happens if I say *"Yes, I want to be in this research"?*

If you agree to participate in this study, you will be randomly assigned to one of the following three groups:

- Time-restricted eating (TRE): This group will receive dietary telephone-based counseling weekly for the first 4 weeks and every 2 weeks thereafter for the 12 week intervention. They will receive counseling to use the myCircadianClock app and will receive weekly text/emails regarding the mCC logging. In addition, this group will have 8 hours where foods of their choice can be eaten. Outside of their window (the fasting period), you can only drink water and eat your medications.

- Caloric Restriction (CR): This group will receive dietary telephone-based counseling weekly for the first 4 weeks and every 2 weeks thereafter for the 12 week intervention. They will receive counseling to use the myCircadianClock (mCC) app and will receive weekly text/emails regarding the mCC logging. In addition, this group will be given options to help reduce the amount of calories in their diet.
- Unrestricted Eating (non-TRE): This group will receive a single dietary telephone-based counseling session. They will receive counseling to use the myCircadianClock app and will receive weekly text/emails regarding the mCC logging. This group will continue their normal eating patterns.

All groups will use the myCircadianClock (mCC) app to document their food and drink intake for the entire study.

At the beginning and just before finishing the study (about 14 days each time), all participants will wear sensors to measure physical activity, and sleep. For the sugar measurements, you will wear a glucose monitoring sensor, which is a tiny plastic tube attached to a sensor which is placed on your skin, for 14 days to measure the changes in your blood sugar. The continuous glucose monitor is a commercially available product. We will be following manufacturer's recommendations for application and removal, which will be about 14 days. You will be provided the results from the continuous glucose monitoring if you wish.

Your participation would last about 16 weeks, and you would have 1 virtual screening visit, 5 in person study visits at the University of Minnesota, 1 virtual study visit mid-intervention, and 6 phone visits. Of note, you will be asked a screening questionnaire about COVID-19 related exposures or symptoms before any in-person visits (either the day before or the day of the visit). You can expect the following procedures at these visits:

Screening Visit (Virtual)
This visit will last about 1 hour.

- The study staff will discuss this consent form with you.
- After you have signed the consent form, you will access the online app mCC ("My Circadian Clock"), which you will download onto your smartphone. You will be asked to log the food that you eat for 7 days. You will use your smartphone to collect data about your eating patterns. You will take pictures of your food or drink every time you ingest so mething. This information will be time stamped and stored.
- You will report your height and weight.
- You will be asked to answer questions in a survey.

You will receive a call about 10-12 days after your screening visit to let you know if you are eligible to proceed to Visit 1.

Baseline Visit 1 (about 10-14 days after the screening visit at the M Health Clinical Research Unit (CRU))
This visit will last about 1 hour and you will be asked to fast before coming to this visit. Additional screening tests will be performed during visit 1, including: BMI calculation via height/weight, and fasting blood labs. Study-related baseline measurements will be gathered during this visit while we determine your eligibility to continue with the dietary phone calls and Visit 2.

- You will have your height and weight measured.

- You will be asked survey questions about your appetite.
- You will use your smartphone to collect data about your eating patterns using the mCC online app until the end of the study. You will take pictures of your food or drink every time you ingest something. This information will be time stamped and stored. You will receive weekly text/email feedback regarding your mCC logging.
- You will receive a wearable sensor that can measure sleep duration, the quality of your sleep, your basal metabolic rate (how much energy your body uses when you are at rest), and your activity levels. The sensor looks like a wrist bracelet. You will wear this sensor for up to 14 days and will return it to the study team at Visit 2.
- The fasting blood draw (about 3 tablespoons) will include a test to measure anemia, thyroid function, kidney function, and cholesterol, glucose, insulin and HbAlc (a 3 month measure of blood glucose) to determine eligibility for the study. You will be provided these results.
- A continuous glucose monitor will be placed on the skin. A catheter will be inserted into the skin for this procedure. This will be removed about 14 days later at Visit 2.

You will receive a call a few days after Visit 1 to let you know about your results and whether you are eligible to proceed with the study.

Phone Call Visits

Each phone call visit will take about 20-30 minute s. You will receive a total of 6 phone calls. Three calls will occur between Visit 1 and Visit 2 over a 2 week period. Three calls will also occur between Visit 5 and Visit 6 over a 2 week period.

The study team will call and ask you questions regarding the previous day and what you had to eat and drink. We will ask that you refer to the Food Amounts Booklet (FAB) that the study team will give to you.

Visit 2 Baseline (2-3 weeks after Visit 1 at Mariucci and CMRR)

This visit will last about 3 hours and you will be asked to fast before coming to this visit.

- Your wearable sensor will be removed during this visit.
- Your glucose monitor will be removed during this visit.
- You will have your height and weight measured.
- You will have a DEXA scan (fasting required) to measure your body composition at the UMN Laboratory of Integrative Human Physiology (LIHP) at Mariucci. If you are female and you have not had a hysterectomy and are not postmenopausal, a urine pregnancy test will be collected to ensure you are not pregnant before the scan.
- You will have an MRI at the UMN Center for Magnetic Resonance Research (CMRR)/ Center for Clinical Imaging Research (CCIR). (This will take about an hour.)

Visit 3 Baseline (1-7 days after Visit 2 at M Health CRU)

This visit will last about 8 hours.

- Before this visit, the study team will give you a meal to eat at home between 5-6pm the evening before coming to this visit. After this meal you will need to fast (water and medications are allowed) and arrive at 7am on the day of your visit. You will need to continue fasting until the visit has concluded.
- You will be randomly assigned to one of the three study groups after finishing this visit, and you will receive dietary telephone-based counseling based on your group.
- Your height and weight will be measured.

- A glucose clamp will be placed to measure how you use sugars, which will be done at the Clinical Research Unit.
- Glucose Clamp: This will be done to measure how well your body uses sugar, we will have you undergo testing using a glucose clamp. You will receive an infusion of a sugar called glucose. This is a stable isotope (meaning that it is not radioactive) and is found naturally. We will specifically use a stable isotope of labeled glucose (6, 6 2H2 glucose) to see the sugar uptake in the liver or the muscle. A catheter will be inserted into a vein in your hand or arm and will be used for collecting blood samples. A second small tube will be inserted into a vein in your other arm and this will be used for a constant infusion of insulin, potassium, and glucose (sugar). (The total amount of blood drawn will be 105 ml, about 7 tablespoons.)
- An indirect calorimetry test will be performed to look at your oxygen a carbon dioxide levels. You will wear a special facemask for about½ hour this testing to collect the carbon dioxide and oxygen from your breath.
- You may be asked to have 3 urine samples collected over the course of the visit.
- We will use stable isotopes (fat and sugar) which are naturally occurring and not radioactive to trace the glucose and fat usage in your body.
- You will be asked survey questions about your quality of life.

Visit 4 Midpoint Virtual Visit (about 6 weeks after Visit 3)

This visit will take about 30 minutes.

- You will report your height and weight. We will ask you survey questions about your appetite.

Visit 5 (about 4 weeks after Visit 4 at Mariucci &CMRR)

This visit will last about 3 hours and you will be asked to fast prior to coming to the visit.

- Your height and weight will be measured.
- You will be asked survey questions about your appetite.
- You will have a DEXA scan (fasting required) to measure your body composition at the UMN Laboratory of Integrative Human Physiology {LIHP) at Mariucci. If you are female and you have not had a hysterectomy and are not postmenopausal, a urine pregnancy test will be collected to ensure you are not pregnant before the scan.
- You will have an MRI at the UMN Center for Magnetic Resonance Research (CMRR)/ Center for Clinical Imaging Research (CCIR). (This will take about an hour.)
- You will receive a wearable sensor that can measure sleep duration, the quality of your sleep, your basal metabolic rate {how much energy your body uses when you are at rest), and your activity levels. The sensor includes a wrist bracelet and a pod that will be attached to your shoe. You will wear this sensor for up to 14 days and you will return it to the study team at Visit 6.
- A continuous glucose monitor will be applied to your skin. This will be removed at study visit 6 about 14 days later.

Visit 6 End of Study Visit (about 2-3 weeks after Visit 5 at the M Heath CRU)

This visit will take about 8 hours and you will be asked to fast before coming to this visit.

- You will have your height and weight measured.
- The continuous glucose monitor will be removed and returned to the study team.
- The wearable activity sensor will be returned to the study team.

- Before this visit, the study team will give you a meal to eat at home between 5-6pm the evening before coming to this visit. After this meal you will need to fast (water and medications are allowed) and arrive at 7am on the day of your visit. You will need to fast until after this visit has finished.
- You may be asked to have 3 urine samples collected over the course of the visit.
- An indirect calorimetry test will be performed to look at your oxygen a carbon dioxide levels. You will wear a special face mask for about½ hour this testing to collect the carbon dioxide and oxygen from your breath.
- You will have fasting blood draw 135 ml (about 9 tablespoons), testing anemia, thyroid function, kidney function, and cholesterol.
- Glucose clamp will be used to measure how well your body uses sugar; we will have you undergo testing using a glucose clamp. You will receive an infusion of a sugar called glucose. This is a stable isotope (meaning that it is not radioactive) and it is found naturally. We will specifically use a stable isotope of labeled glucose (6, 6 2H2 glucose) to see the sugar uptake in the liver or the muscle. A small tube, called a catheter, will be inserted into a vein in your hand or arm and will be used for collecting blood samples. A second small tube will be inserted into a vein in your other arm and this will be used for a constant infusion of insulin, potassium, and glucose (sugar). (The total amount of blood drawn will be about 8 tablespoons.)
- We will use stable isotopes (fat and sugar) which are naturally occurring and not radioactive to trace the glucose and fat usage in your body.
- You will be asked survey questions about your quality of life.

An optional survey will be emailed to you via email 1 month, 3 months, and 6 months, after the intervention to follow-up on the study. See the optional section at the end of this consent form to let us know if you would like to receive the survey.

The experimental treatment you get will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose what experimental treatment you get.

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

If you take part in this research, you will be responsible for:

- Coming to the study visits
- Answering the surveys as best as possible
- Participating in study procedures
- Tracking food intake

What happens if I say "Yes", but I change my mind later?

If you take part in this research study, and want to leave, you should tell us. Your choice not to be in this study will not negatively affect your right to any present or future medical care.

We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

If you stop being in the research, information about you that has already been collected may not be removed from the study database.

Can I be removed from the research?

It's possible that we will have to ask you to leave the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

Blood Sample:

Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.

Continuous Glucose Monitor:

The monitor attaches to your skin with adhesive. Upon initial insertion, we will use a small disposable needle to initially attach the monitor to your body. After the initial attachment, the needle will be removed and the monitor will sample blood through a small plastic catheter. There may be a risk for bleeding or bruising when initially placing the continuous glucose monitor. You will wear this monitor for about 14 days. Side effects include a rash to the sensor adhesive, or the sensor might not stay securely on your skin. Please tell your study doctor if you have any skin/tape allergies they should be aware.

Glucose clamp:

During the glucose clamp, the injection of insulin has a risk for causing low blood sugar. If you have low blood sugar, you may feel hungry, sweaty and weak. However, intravenous sugar will be given at the same time as the insulin, with regular measurement of the blood sugar level. With the constant presence and supervision of a doctor and nurse, the likelihood of a low blood sugar reaction is extremely low. If the symptoms of low blood sugar should occur or if the blood sugar levels are low as determined by the laboratory testing, the rate of the intravenous sugar infusion will be increased immediately to correct this problem.

DEXA Scan:

As part of this study, you will undergo two DEXA scans, one at Baseline and one at Week 10. This procedure involves exposure to ionizing radiation. This radiation exposure is not necessary for your medical care and is for research purposes only. The average amount of radiation that the average person would receive from this procedure is less than 1% of that received from natural sources of radiation by a Minnesota resident in one year (3 mSv). This exposure involves minimal risk and is necessary to obtain the research information desired.

Dietary Recall:

There is a risk about breach of confidentiality. Study staff will call participants and ask about dietary intake for the last 24 hours. The actual call will be unannounced but there will be 3 calls within a specified 2 week window. Participant will be aware of the 2-week window. This will occur 2 times during the study.

Documentation of eating events using the my Circadian Clock application:

All documented eating events (time, image) will be stored and sent deidentified as per Salk Institute protocols. By consenting to this study, you are also consenting to use mCC app and also allowing the Salk research team to share data from the mCC app with our team.

- **myCircadianClock smartphone application (mCC app).**

- The mCC app was created by and managed by Dr. Satchidananda Panda's lab at the Salk Institute for Biological Studies. It is HIPAA compliant and double-encrypted. Consenting to use and using the mCC app is necessary and critical for participation in the study.

- **Activities.**
  - The myCircadianClock app may ask you to: Answer survey questions about your health behaviors, record what you eat or drink.
  - The app sends occasional reminders to complete study activities.
  - Educational material may be sent through the app.
- **Sensor and health data**
  - This study can gather sensory data from your phone if you allow it to upon installation.
  - The app will also use the built in GPS sensor to tag the location only when you log your data. This will help you to track what and where you eat, which may help you adjust your diet. It helps the research to account for any unusual change in your eating or sleeping pattern due to a change in time zone when you travel. Change in time zones or moving to a different latitude within the same time zone can change the local sunrise and sunset time or local day-length, which can affect your circadian clock for a few days.
  - The use of the myCircadianClock app is not intended to evaluate your health and is not a diagnostic test. If you are concerned about any aspect of your health, you should consult with your physician.
- **Data Gathering**
  - Our daily pattern of activity, sleep, and eating changes with season, latitude, work schedule, and travel. Collected data may reveal how daily behaviors affect your quality of life and body weight, and also advance clinical research into circadian rhythms.
  - Learn more: myCircadianClock helps you keep track of health behaviors such as diet, activity, sleep and taking your medications or supplements.
  - Data that you share through the app as part of the research study will create an unprecedented large-scale database of daily behaviors and health provided by people just like you.
  - Studying this real-world data will help researchers understand how daily behaviors influence health in real life, with a resolution never achieved before. (Traditionally, these studies are done by asking people to recall answers to very long questionnaires on paper).
  - At the same time, myCircadianClock analyzes your data to provide personalized insights into how your daily eating, sleeping and activity patterns relate to your overall health, and can help you maintain a healthy lifestyle. Since the feedback is determined from multiple days of your routine behavior, some of these insights will be accessible in your phone after two weeks of data collection.
  - To improve data collection, the app may send you a reminder and push notifications. If you do not want to be bothered with these reminders, you can turn this option off.
  - By combining a personal app and a research study, myCircadianClock will help explore how the smartphone may be used with new kinds of clinical research in the future.
- **Privacy**
  - The following personal health information will be collected from you by the app: email address, country, language, photos of food/beverages you take, activity/exercise, sleep, and health entries, timestamp of entries, and geographic location data from entries.
  - Your data will be sent to a secure database where it will be separated from your personal identity.
  - We take several steps to protect your privacy and the privacy of your app data.
  - App-generated data is associated only with a random study code, and this code is used in all future analyses separating it from any personally identifiable information.

- These steps ensure that researchers analyzing the coded study data will not be able to connect it to any individual user.
- Whenever app data is transferred to a research study computer, it will be encrypted so that others cannot interpret the data or associate it back to you.
- Encrypted app data (stripped of personal identifiers, and associated only with a random code) will be sent to secure data servers used for the myCircadianClock research study.
- Study investigators chose Amazon Web Services for this important responsibility because they are a world leader in the secure storage and protection of sensitive data. They have a proven track record of safeguarding and managing potentially sensitive biomedical data in accordance with regulations that govern human research and medical information (e.g., regulations mandated by Institutional Review Boards [IRB] and the Health Information Portability and Accountability Act [HIPAA]).
- We will de-identify your data and use secure computers, but we cannot ensure complete privacy.
- One potential loss of privacy would be if someone sees your data from myCircadianClock on your smartphone. For security, myCircadianClock suggests that your smartphone be protected either by a passcode or fingerprint sensor. This ensures that only you can enter and use the app.

- **Utilizing Data**
  - Your coded data will be used for research and may be shared with other researchers.
  - Study investigators will analyze coded (no personal identifiers) app data from everyone who agrees to participate in the myCircadianClock study, but they will be unable to connect it back to any individual user.
  - The results of this research may be published in a scientific or medical research journal so that others can learn from this study. Results will never be published in a way that would allow data to be associated with individual users.
  - After this study is completed, other researchers may request access to the coded study data (already stripped of personal identifiers), so that it can be analyzed in a new way to benefit medical research . Those requesting data must agree to use the data for research responsibly and in accordance with applicable regulations; these data requests will be reviewed by a group of study investigators. Amazon Web Services will have no oversight over future research conducted with coded study data.
  - Other researchers who are granted access to coded study data will not be able to connect the data back to you.
  - Study data will never be sold to any third party.
- **Issues to Consider**
  - Your participation in this study will take 5-10 minutes per day on average. Entering information and responding to surveys should take on average 2-3 minutes each day. Occasionally, tasks may take a few minutes longer (e.g.,a longer questionnaire).
  - Participation in this study does not require you to change anything related to your smartphone account or data plan. However, your phone must have data or wifi capability and must connect to internet in order to transmit data to our servers. The app can use either an existing mobile data plan or Wi-Fi connections: you may configure the app to use only Wi-Fi connections if you wish to limit impact on your data usage.
- **Safety and Legality**
  - As with any smartphone app, follow prevailing laws about when and where you use your smartphone. Similarly, follow local and federal regulations about the usage of a smartphone in specific areas.
  - Additionally, the app should not be used in any capacity to perform or document illegal activity. The Salk Institute for Biological St u dies, Dr. Satchidananda Panda and all members of his research team,

including collaborators, are not liable for any illegal activity that is performed, captured, or stored by the myCircadianClock app.

- **Study Survey**
  - Some of the tasks in this study will require you to answer survey questions about various health and lifestyle factors.
  - myCircadianClock will collect some of its data on your health behaviors through short survey questions, such as: Did you forget to eat breakfast today? When did you wake up this morning? Do you feel sleepy during the day?
  - For dietary information, myCircadianClock will prompt you to take pictures of every food, beverage, water, medication, and supplement(s) you take.
  - When picture taking is difficult or socially awkward as in a meeting, if you forgot to take picture or you are repeatedly eating the same item, you can also enter the information textually from a different screen.
  - In general, more data entered into the app results in more accurate and informative personalized insights.
- **Study Tasks**
  - Although this is not required by the study, you have the option of including health information in the app, including activity (step counts/distance), heart rate, height and weight, you can sync other smartphone apps and sensory devices (such as Apple Health Kit and Google Fit) with myCircadianClock. You also have the choice to allow the myCircadianClock app to access your location in order to determine the local time. You can allow or deny these features when you first install the myCircadianClock app, and are able to change these settings at any time.
  - All data entered is used solely for tracking purposes, not diagnosis. The Salk Institute for Biological Studies, Dr. Satchidananda Panda and his lab are not responsible for providing medical advice and are not liable for your medical care. You should contact a medical professional for medical advice.
  - The myCircadianClock app provides personalized feedback in the form of graphs and text to display your progress, and provide insights into your health behaviors.
  - The app summarizes data about how food, sleep or activity patterns in specific time of the day are associated with your health and wellbeing. These insights may help you understand your health behaviors better, and help you manage your health. Viewing the graphs and text is optional but may be useful or interesting to you.
  - In your Profile within myCircadianClock, you can set reminders for yourself to complete app activities. In general, more data entered in the app results in more accurate and informative insights.
- **Meals, activity, and sleep:** The smartphone application myCircadianClock (mCC app) will serve as an electronic food, activity, and sleep diary.
  - On the server side, a sub-study dashboard will be created for this specific project. Clinical coordinators from Dr. Chow's research team will have password-protected access to the study data. In the study summary dashboard, your study code and the date of activation of the app will be shown along with your daily log. If you fail to log any food data for more than 1 day, the dashboard flags you and sends an alert to the coordinator. The coordinators will login to the dashboard at least twice weekly to monitor food intake data, and follow up with you as necessary.
  - If you are randomized to the time-restricted eating arm, you will self-select an interval of 8 hours per day within which to consume your food. You can easily track your progress of the daily eating pattern with the time-stamping feature of the app that offers a visual summary.

- If you have any difficulty logging data, or have questions about any of the features of the app, you will be able to contact the study coordinator through the feedback feature of the app. The questions will be delivered to a HIPAA compliant email server specifically set up for this study.

Use of stable isotopes of glucose and fat:
These are naturally occurring and not radioactive. Possible nausea and discomfort associated with infusion.

Indirect calorimetry:
Possible discomfort associated with the face mask. A face mask will be use to noninvasively collect breath samples to measure sugar and fat burning.

Breach of Privacy:
There is some risk of a data breach involving the information we have about you. We comply with the University's security standards to secure your information and minimize risks, but there is always a possibility of a data breach.

MRI:
MRI machines: use a strong magnet and radiofrequency magnetic fields to take images of your body. The scanning process is similar to an x-ray or CT scan, but MRI does not use ionizing radiation (high-energy radiation that can potentially cause damage to DNA) like x-rays or CT scans.

The risks associated with MRI scans are:

Projectiles: Objects with magnetic properties can be pulled into the magnet and turn into projectiles. To minimize this risk we ask that subjects remove all metallic items (watches, cell phones, hair pins, etc.) prior to entering the scanner and by controlling access to the scanner.

Claustrophobia: The scanner is a long narrow tube that may cause some people to feel claustrophobic.

Hearing Damage: The noise generated by the operation of the scanner during a study is loud enough to cause hearing damage if you do not wear hearing protection. Hearing protection is required and is provided by the investigator.

Nerve Stimulation: Some people experience localized tingling, twitching, or muscle contractions during MRI scans. This is expected, but if it is uncomfortable please notify the research staff.

Disruption of Devices: Some devices can be damaged by magnetic fields and should not be brought into the scanner room. This includes some implanted devices such as pacemakers, cochlear implants, insulin pumps, nerve stimulators, etc. If you have any implanted device notify the research staff.

Heating of Devices: The radiofrequency waves used in MRI can heat conductive materials such as metal implants (screws, plates, rods, wires, artificial joints, etc.), certain tattoo inks, certain clothing fabrics, jewelry, medication patches, wigs, etc. You will be asked to remove these items if possible. If they cannot be removed you will be asked to provide more information to allow MRI staff to be able to make determination on the safety of proceeding with the scan.

A thorough pre-scan questionnaire will allow us to minimize the risk of device disruption and heating. You will be in constant contact with the research staff and should notify the research staff immediately, via the squeeze ball, if you notice anything unusual, become claustrophobic, think that your hearing protection is not adequate, or if you experience nerve stimulation that is uncomfortable.

In addition, there is a risk of unknown effects related to participation in MRI research. Long-term effects of exposure to high magnetic fields are unknown. Most people experience no short-term ill effects from the strong magnetic field, but some people report dizziness, mild nausea, headache, a metallic taste in their mouth, or sensations of flashing light s. These symptoms, if present, subside shortly after leaving the magnet. If any sensations experienced during participation cause discomfort or pain, notify the research staff right away and your participation will stop and you will be taken out of the magnetic field.

Will I receive any imaging results after an MRI?
The pictures created during this study are for research purposes only and are not intended to provide health care to you. The investigator in charge of this study has decided that results from your scan will not be shared with you or your physician.

What do I need to know about reproductive health and/or sexual activity if I am in this study?
The risks of exposure to high magnetic fields are unknown for fetuses. Therefore, if you are a female who is capable of becoming pregnant, and you have any reason to believe that you might be pregnant, you should not participate in this study.

Will I know about any new information about the effects of MRIs on human health?

Notification of Significant New Findings
You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

What happens to the information collected for the research, including my health information?

We try to limit the use and sharing of your information, including research study records, any medical records and any other information about you, to people who have a need for this information. But we cannot promise complete confidentiality.

Overview

If you participate in this study, your information, including your health information, will be used and shared for purposes of conducting this research. As described later in this Consent Form, your information may also be used and shared for publishing and presenting the research results, future research, and any optional elements of the research you agree to in this Consent Form, which may include creating audio and video recordings of you. If you sign this Consent Form, you are giving us permission to use and share your health information for these purposes, and if we are using your

medical records, you are giving permission to any health care providers who are treating you to share your medical records with us.

What health information will be made available?

Health information about you to be used and shared for the research includes those items checked by the research team below:

Your medical records, which may include records from hospital and clinic visits, emergency room visits, immunizations, medical history and physical exams, medications, images and imaging reports, progress notes, psychological tests, EEG/EKG/ECHO reports, lab and pathology reports, dental records and/or financial records. These records may be used and shared for as long as this research continues.

Information collected as part of this research study, including research procedures, research visits, and any optional elements of the research you agree to, all as described in this Consent Form. This information might not be part of your medical record, and may include things like responses to surveys and questionnaires, and information collected during research visits described in this Consent Form.

What about more sensitive health information?

Some health information is so sensitive that it requires your specific permission. If this research study requires any of this sensitive information, the boxes below will be marked and you will be asked to initial to permit this information to be made available to the research team to use and share as described in this Consent Form.

☐ My drug & alcohol abuse, diagnosis &treatment records_____(initial)

☐ My HIV/AIDS testing records_____(initial)

☐ My genetic testing records_____(initial)

☐ My mental health diagnosis/treatment records_____(initial)

☐ My sickle cell anemia records_____(initial)

Who will access and use my health information?

If you agree to participate in this study, your information will be shared with:

- The University of Minnesota research team and any institutions or individuals collaborating on the research with us;
- Others at the University of Minnesota and M Health/Fairview who provide support for the research or who oversee research (such as the Institutional Review Board or IRB which is the committee that provides ethical and regulatory oversight of research at the University, systems administrators and other technical and/or administrative support personnel, compliance and audit professionals (Such as the Quality Assurance Program of the Human Research Protection Program (HRPP)), individuals involved in processing any compensation you may receive for your participation, and others;
- The research sponsor(s), any affiliates, partners or agents of the sponsor(s) involved in the

research, organizations funding the research, and any affiliates, partners or agents of the funding organization(s) involved in the research;

- National Institute of Health (NIH)Organizations who provide accreditation and oversight for research and the research team, and others authorized by law to review the quality and safety of the research (such as U.S. government agencies like the Food and Drug Administration, the Office of Human Research Protections, the Office of Research Integrity, or government agencies in other countries); and
- Organizations that process any payments that may be made to you for participating in this study, and any other individuals or organizations specifically identified in this Consent Form.

Additional sharing of your information for mandatory reporting

If we learn about any of the following, we may be required or permitted by law or policy to report this information to authorities:

- Current or ongoing child or vulnerable adult abuse or neglect;
- Communicable, infectious or other diseases required to be reported under Minnesota's Reportable Disease Rule;
- Certain wounds or conditions required to be reported under other state or federal law; or
- Excessive use of alcohol or use of controlled substances for non-medical reasons during pregnancy.

How will my information be used in publications and presentations?

We may publish the results of this research in scientific, medical, academic or other journals or reports, or present the results at conferences. Information that makes it easy to identify you (such as your name and contact information, SSN and medical records number) will not be part of any publication or presentation. If you have an extremely unique or rare condition that is not shared by many others, it is possible that some people may be able to determine your identity even without these identifiers.

What will be done with my data and specimens when this study is over?

We will use and may share data and/or specimens for future research. They may be shared with researchers/institutions outside of University of Minnesota. This could include for profit companies. We will not ask for your consent before using or sharing them. We will remove identifiers from your data and/or specimens, which means that nobody who works with them for future research will know who you are. Therefore, you will not receive any results or financial benefit from future research done on your specimens or data.

Do I have to sign this Consent Form and give my permission to make my information, including my health information, available for use and sharing?

No, you do not have to sign this Consent Form. But if you do not sign, you will not be able to participate in this research study. Treatment available outside of the study, payment for such treatment, enrollment in health insurance plans and eligibility for benefits will not be impacted by your decision about signing this Consent Form.

Does my permission for making my health information available for use and sharing ever expire?

No, there is no expiration date.

May I cancel my permission for making my health information available for use and sharing?

Yes. You may cancel your permission at any time by writing to the researcher at the address on the first page of this Consent Form. If you cancel your permission, you will no longer be in the research study.

You may also want to ask someone on the research team in canceling will affect any research related medical treatment. If you cancel your permission, any health information about you that was already used and shared may continue to be used and shared for the research study and any optional elements of the study to which you agree in this Consent Form.

What happens to my health information after it is shared with others?

When we share your information with others as described in this Consent Form, privacy laws may no longer protect your information and there may be further sharing of your information.

Will I be able to look at my records?

It is possible that the research team may not allow you to see the information collected for this study. However, you may access any information placed in your medical records after the study is complete.

Certificate of Confidentiality

To help protect your privacy, the National Institutes of Health has granted a Certificate of Confidentiality. The researchers can use this Certificate legally to refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate does not prevent a researcher from reporting information learned in research when required by other state or federal laws, such as mandatory reports to local health authorities for abuse or neglect of children/vulnerable adults, or information to the Food and Drug Administration (FDA) when required in an FDA audit. However, the Certificate limits the researcher from disclosing such information in follow up civil, criminal, legislative or administrative legal proceedings if the information was created or compiled for purposes of the research.

You also should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

A description of this clinical trial will be available at http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include your name or any other direct identifiers such as your contact information. The Web site may include a summary of the results of this research. You can search this Web site at any time.

Will I receive research test results?

Most tests done on samples in research studies are only for research and have no clear meaning for health care. However, you will be provided test results which may be clinically relevant (i.e. body composition, glucose monitoring results, screening lab results).

Will anyone besides the study team be at my consent meeting?

You may be asked by the study team for your permission for an auditor to observe your consent

meeting. Observing the consent meeting is one way that the University of Minnesota makes sure that your rights as a research participant are protected. The auditor is there to observe the consent meeting, which will be carried out by the people on the study team. The auditor will not document any personal (e.g. name, date of birth) or confidential information about you. The auditor will not observe your consent meeting without your permission ahead of time.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/ participants. You are encouraged to contact the HRPP 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.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Will I be compensated for my participation?

If you agree to take part in this research study, we will pay you for your time and effort. All study tests, procedures, and materials are provided to you free of charge.
Payment Schedule:

Visit	Payment
Screening Visit *(virtual)*	$10
Visit 1 *(in person)*	$15
3 dietary phone call completion	$25
Visit 2 *(in person)*	$50
Visit 3 *(in person)*	$100

Visit 4 *(virtual)*	$25
Visit 5 *(in person)*	$50
3 dietary phone call completion	$25
Visit 6 *(in person)*	$100

If you complete the entire study (screening visit to final visit), your total compensation will be $400. If you do not complete all study visits, your compensation will be less than the total amount, based on how many visits you completed.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I Agree	No, I disagree	
		The investigator may email me the optional post-intervention survey at 1, 3, and 6 months, as discussed earlier in this form. This is only for the TRE and CR groups.
		The investigator may contact me in the future to see whether I am interested in participating in other research studies by Lisa Chow.
		We would like your permission to store your blood, urine, and muscle samples for future testing in order to better understand diabetes and insulin resistance. These samples will be stored indefinitely using a unique code without personal identifiers. Dr. Chow will be custodian of these samples. This means that she will manage the use of these samples. Results from testing these future samples will not be given to you. No genetic studies will be performed on these samples.

SIGNATURES:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent