COMIRB
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Principal Investigator: Corey Rynders, PhD
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Study Title: Time Restricted Feeding and Metabolic Rhythms in Humans
Short title: The Metabolic Rhythm study

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
This study plans to learn more about how daily eating patterns affect health and determine risk for various chronic diseases such as obesity and diabetes.

In this study, we want to find out if restricting food intake to a short window during waking hours (i.e., time restricted feeding) changes metabolism in a manner that protects against obesity and diabetes. Specifically, we want to see if the benefits of time restricted feeding are due to how the body uses fats for fuel. We also want to see if altering meal timing influences daily physical activity patterns and sleep.

You are being asked to be in this research study because you are an adult male or female between the ages of 20 to 50 years old and report consuming food over a 12-hour period during daytime hours.

The results from this study may help us to understand whether meal timing is an important factor in obesity and diabetes treatment and prevention. Knowing this information may also help to develop therapies such as time restricted feeding to prevent long term diseases in men and women.

Other people in this study
Up to 50 people from your area will participate in the study.

What happens if I join this study?
If you agree to join the study, you will be asked to come to the CTRC (Clinical Translational Research Center) for all of your study visits (**4 visits total**). There is **1 screening visit**, **1 baseline visit**, and **2 inpatient study visits.** Visits will be located in either the CTRC outpatient clinic (3rd floor of the Leprino Building at the Anschutz Medical Campus), or the CTRC inpatient clinic (12th floor of the University of Colorado Hospital (UCH), Anschutz Inpatient Pavilion). For 1 week before each inpatient study visit, you will be asked to eat food at specific times, consume a special diet prepared by the CTRC Metabolic Kitchen, and wear monitors to measure your blood glucose, sleep and activity patterns. Each inpatient study visit involves 3 consecutive overnight hospital stays. The study procedures that will be performed are identical between the 2 inpatient

study visits. The only difference is a feeding schedule that the researchers will ask you to follow.

Screening Visit
You will be asked to complete a screening visit to determine if you are eligible and if it is safe for you to participate in this study.

The table below is a rough outline of the screening procedures. The paragraphs under the table describe the procedures in more detail.

Visit # 1	Study Procedures & Instructions	Length of Visit
Screening	• Review and sign informed consent • Blood draw* • Medical history & Physical exam • Questionnaires about sleep, diet, and activity ** 8-10 hour fast (no food or caffeine, only water) before visit*	1.5 hours

- Medical history and physical exam: A physical examination and medical history will be done by a study physician or nurse involved in the study at one of your screening study visits. Your Informed Consent to participate in the study will also be gathered at this time, if you agree.

- Blood draw: This will involve collecting approximately 1 Tablespoon of blood and will take about 10 minutes. The blood tests measure blood cell count, electrolytes, liver and kidney function. You will be asked to fast (nothing to eat or drink, except water) for 8-10 hours prior to the visit.

- Questionnaires: We will ask you to answer questions about your sleep habits, eating habits, risk of sleep disorders, risk for depression and anxiety, and your physical activity level. We will ask you to maintain your regular sleep patterns for the time you are in the study.

Baseline Visit
If you are eligible after the screening visit you will be asked to complete a baseline assessment of your body composition, metabolic rate, patterns of food intake, sleep, glucose, and activity.

Visit # 2	Study Procedures & Instructions	Length of Visit
Baseline #1	• DXA • Resting metabolic rate measurement* • Receive devices for assessment of physical activity, sleep, glucose, and meal timing ** 8-10 hour fast (no food or caffeine, only water) before visit*	1.5 hours

- DXA: We will measure total body fat using a machine called a DXA. These tests will require lying still on a table for about 10 minutes.

- Resting metabolic rate: You will have your resting metabolic rate measured using a metabolic cart. This measurement will tell us how many calories your body requires each day to maintain your current body weight. This measurement takes about 20 minutes and requires you to lie in a hospital bed and rest quietly while a clear plastic hood is placed over your head. This hood will collect the air you breathe, which will then be used to determine your calorie requirement.

- Assessments of free-living meal timing, sleep, glucose, and activity:

    - For 7 consecutive days you will wear devices on your wrist (Actiwatch) and thigh (ActivPAL) that measure your activity patterns and sleep.
    - You will track your meals and meal times by taking photographs and texting them to a secure Google Voice account. You will continue tracking this for 7 consecutive days. While tracking this information, you will be asked questions related to appetite and eating behaviors.
    - For 7 days you will wear a device called a continuous glucose monitor that measures your glucose levels every 15 minutes. The glucose monitor has a flexible tip that is inserted just under the skin in your upper arm. The monitor should be worn continuously during the 7-day study period even when showering.

Study Phases and Inpatient Study Visits
After the baseline assessments you will be asked to complete **2** study phases in a randomized order. Each study phase consists of a specific feeding condition that will last 7-days. Each study phase will be separated by a minimum 8 week wash-out period. These study visits include a hospital stay, which includes 3 overnights, per visit. The feeding conditions are:

1. **Early Time Restricted Feeding (E-TRF):** Consume meals over an 8-hour window during the beginning of waking hours. Meals will be consumed at individually prescribed times based on your habitual sleep schedule.
2. **Late Time Restricted Feeding (L-TRF):** Consume meals over an 8-hour window during the end of waking hours. Meals will be consumed at individually prescribed times based on your habitual sleep schedule.

Study Days and Visits:
The table below shows a rough outline of the procedures you will complete for each study phase (E-TRF and L-TRF). The paragraphs under the table describe these visits and procedures in more detail. The only difference between the two conditions is the feeding schedule. All other experimental procedures are identical.

Visits #3 and #4	Study Procedures & Instructions	Length of Visit & Location
Day 0 Device Pick-up	• Pick up sleep and activity monitors • Study team hooks up continuous glucose monitor	15 minutes
Days 1 – 3 Diet Pick-up	• Maintain a consistent 8-hour sleep schedule • Consume meals at prescribed times during the day • Text photographs to track meals • Complete written logs • Pick up 3-day outpatient diet from the CTRC kitchen on day 3	Outpatient (at-home) 0.25 hours required to pick up meals from CTRC on day 3
Day 4 - 5	• Maintain a consistent 8-hour sleep schedule • Consume study diet at prescribed times during the day • Text photographs to track meals • Complete written logs	Outpatient (at-home)
Day 6 First overnight.	• Continue to maintain a consistent 8-hour sleep schedule; Consume study diets at prescribed times during the day*;* Text photographs to track meals; Complete written logs • Check into the inpatient CTRC in the evening • First night sleep study	Outpatient (at-home) Inpatient CTRC **check-in about 3 hours prior to bedtime*
Day 7 Second Overnight.	• 23-hour whole room calorimeter stay • Frequent blood draws • Second night sleep study • Questionnaires • Urine collection	Inpatient CTRC 24.0 hours
Day 8 Third Overnight.	• “Constant routine” protocol to measure rhythms in metabolism (Note this protocol involves lying in bed for 30-hours in dim light, eating a snack every hour, and no sleep is permitted. You will be able to watch TV, read, play games, or do crafts to pass the time). • Frequent blood draws • Frequent resting metabolic rate	Inpatient CTRC 24.0 hours

	measurements • Urine collection • Questionnaires	
Day 9 Discharge.	• 8-hour sleep opportunity to recover from sleep restriction protocol • Discharge from CTRC in the afternoon • Transportation must be arranged (you will not be allowed to drive yourself)	Inpatient CTRC

- Outpatient (at-home) sleep and activity control (Days 1 - 6): For each study phase, you will record your sleep and wake times for all days leading up to your inpatient study day. You will be asked to choose a consistent bed time and wake time with lights off for at least 8 hours during each night. To verify this, you will each wear devices on your wrist (Actiwatch) and thigh (ActivPAL) that measure your activity patterns and sleep. You will use a written diary to log your sleep times.

- Outpatient (at-home) meal timing control (Days 1 - 6): For each study phase you will be asked to consume meals at specified times for all days prior to your inpatient visit. The specific meal times will be provided by the study team and will be scheduled based on your usual sleep-wake patterns. The study team will provide you with dietary guidelines to follow during the first 3 days (Days 1-3), but you will be responsible for providing and preparing your own food during these days. The study team will provide you with food during the last 3 days (Days 4-6) as described in more detail below. To verify that you are consuming meals at specific times you will track everything you eat by texting photographs to a secure Google Voice line.

- Continuous glucose monitoring: You will wear a sensor that measures your blood glucose levels during each study phase. The sensor has a flexible tip that is inserted just under the skin in your upper arm. The sensor should be worn continuously even when showering.

- Outpatient (at-home) diet (Days 4-6): During the 3 days leading up to each hospital stay you will be given a control diet prepared by the CTRC metabolic kitchen. You will take home enough prepared food to last for the entire 3 days. You will be asked to eat only the food provided by the dieticians.

- CTRC check-in and sleep study (Evening of Day 6): In the evening of Day 6 you will be admitted to the University of Colorado CTRC in the evening for a sleep study and your first overnight hospital stay. You may bring items you use for your bedtime routine, and you can sleep in your own nightclothes. The room where

your sleep study is done is called a whole room calorimeter and is designed to measure your metabolism while you sleep. The room calorimeter is the size of a dorm room and has a bed, bathroom, and privacy shades. The room has a video camera, so the CTRC staff can see what's happening in the room when the lights are out, and an audio system, so they can talk to you and hear you from their monitoring area outside the room. You can turn off the video camera from inside the room for privacy whenever necessary. After you get ready for bed, a member of the study team will attach sensors to your body to keep track of a number of body functions during sleep, such as: brain waves, breathing rate, heart rate, eye movements, leg movements, blood oxygen levels, and jaw or chin movements. The sensors are wireless in case you need to get up at night. Someone from the staff will be available to you throughout the night.

- Room calorimeter study (Day 7): In the morning when you wake up, a member of the staff will enter the room calorimeter and place an intravenous catheter (hollow plastic tube) in a vein in one of your arms. The IV catheters will be used to take frequent blood samples (about every hour) during the room calorimeter stay. You will remain in the room calorimeter for 23 hours until the next morning. During the day you will have your blood draw, complete short walking sessions at specified times and consume a study diet at specified times. At night you will have your sleep measured again, similar to your first night on the CTRC.

- Dietary fat tracer: You will be asked to consume a milk shake that contains a fat tracer with the first meal of the day. There is no known risk with the use of the stable isotopes. They are not associated with allergic responses as they are substances normally present or produced in the body.

- Constant routine protocol (Days 8): To measure biological rhythms in your blood we will use a study protocol known as the “constant routine”. You will remain in bed with minimal activity (only to use the bathroom) for a period of 30 hours. The room will be dimly lit and you will receive hourly snacks for 30 hours. You will not be able to sleep for the entire 30 hours. You may watch TV, read and talk to the members of the study team during the protocol. A member of the study team or nursing staff will be with you at all times to keep you company and make sure you stay awake. During the 30h period we will draw blood samples, wear sensors on your body to measure your skin temperature, and have your metabolic rate measured about every 2 hours.

- Urine collection: For the entire time you are on the inpatient CTRC, we will collect all urine that you produce over the entire time you are in the metabolic chamber. Any time you need to urinate, you will do so in a specified collection jug.

- Body Temperature: Your skin temperature will be monitored throughout the inpatient period using iButton devices placed below your collar bone, on your wrists, and feet. Each iButton device is a computer chip enclosed in a small case

the size of a button. The iButtons are attached directly to the your using medical tape.

- Saliva sample: Every hour during the constant routine protocol we will collect a sample of your saliva to measure hormones (melatonin and cortisol) that are biological markers of time.

- Appetite ratings: About every hour the study team will ask you questions about your appetite and desire for certain types of food (e.g., sweet, salty, etc.).

Note: In the event of a public health emergency, natural disaster, severe weather, or for other compelling reasons at the discretion of the study PI, some study visits may be held by Zoom videoconference or phone call and may not follow the exact timeline outlined in the protocol. Consent may be performed virtually (rather than in person) if needed for participant safety. Under these circumstances, study outcome measure visits may be delayed, postponed or cancelled as necessary for participant/staff safety and thus may not follow the exact timeline outlined in the consent.

What are the possible discomforts or risks?

There are certain risks and discomforts that may be associated with this research. They include:

- **Risks of DXA scan -** As part of this study we will perform 1 DXA scan of your whole body. DXA is a way of looking inside the body by using X-rays. X-rays are a type of radiation. Your natural environment has some radiation in it. This DXA will give you about the same amount of radiation that you would get from your environment in 2 days.
- **Risks of catheterizations -** Blood will be drawn hourly through an IV catheter during the inpatient visits. There is a potential risk of a blood clot in the vein with the catheter placement but this risk is small. Local hematomas are also possible but infrequently observed. There is a slight risk of infection with the blood draw. A small amount of heparin will be used to allow us to sample blood while the catheter is in place. Heparin works by preventing blood clots from forming in IV catheters when they are not in use. Allergic reactions and side effects to heparin are rare. You should not use heparin if you are allergic to heparin or pork products. Symptoms of an allergic reaction to heparin may include, rash, itching or swelling at the IV catheter site, dizziness or trouble breathing.
- **Risk and possible discomforts of having blood taken -** The total amount of blood taken will be approximately 500 mL (about 2 1/4 cups) during each inpatient stay. This is equal to a maximum of 8.0% of total blood volume for any one test day, and is not a risk for anemia. Inpatient visits will be separated by 8 weeks for safety purposes. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when

the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

- **Sleep loss.** You may not sleep as well as you normally do during the inpatient study visits. Short sleep is known to reduce daytime alertness and executive function. In addition, we are completely restricting your sleep for one of the inpatient nights. Because of this you will not be allowed to drive yourself home from these visits.
- **Risk of nickel allergy-** The temperature sensors that we will place on various areas of your skin are made of nickel and my cause a rash if you have a known nickel allergy.
- **Risk and possible discomforts of continuous glucose monitoring-** The risks of using the system are low but may include pain or discomfort, bleeding, or bruising during sensor insertion or removal. Local infections at the insertion site are extremely rare. Users may experience inflammation, irritation, itching, or skin discoloration from wearing the adhesive patch.
- **Risk of loss of privacy/ confidentiality -** There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.
- The study may also include risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about how meal timing influences metabolism and risk for chronic diseases. This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Who is paying for this study?

This research is being sponsored by a mentored career development grant from the National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to Corey Rynders, PhD.

Will I be paid for being in the study?

You will be paid $25 for the baseline visit and $500 per inpatient room calorimeter visit. This will add up to a total of $1025 if you complete all of the visits. It will take at least 3 weeks from the time the study ends to process this monetary compensation. If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed.

The study is willing to offer monetary incentive for participants who are willing to schedule inpatient visits that occur on a greater number of weekdays. This is to help assist with missed compensation due to missed workdays. If you have to miss more than 1 day of work on a weekday, then you will be compensated an extra $75 per inpatient visit. This could increase total compensation up to $1175.

It is important to know that payments for participation in a study is taxable income.

Will I have to pay for anything?

It will not cost you anything to be in the study.

Is my participation voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, for failing to follow study protocol (for example not following meal timing, sleep timing etc.) or for any other reason.

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call Dr. Dan Bessesen the study physician immediately. His pager number is 303-266-4361. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Corey Rynders, Ph.D. You may ask any questions you have now. You may have questions about your rights as someone in the study. You can call Dr. Rynders with questions. If you have questions, concerns, or complaints later, you may call Dr. Rynders at 720-848-6461. You will be given a copy of this form to keep.

While your primary source of information pertaining to participation in this study is the principal investigator (Corey Rynders, PhD), a Research Subject Advocate is also available on the Clinical Translational Research Center at (720) 848-6662 to answer questions relating to participation in this study. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

Certificate of Confidentiality

This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. The Certificate prohibits the researchers from disclosing your name, or any identifiable information, document or biospecimen from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings.

These protections apply only to your research records. The protections do not apply to your medical records.

The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:

- To those connected with the research,
- If required by Federal, State or local laws,
- If necessary for your medical treatment, with your consent,
- For other scientific research conducted in compliance with Federal regulations,
- To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or

- Under other circumstances with your consent.

A Certificate of Confidentiality does not protect information you or a member of your family voluntarily release.

Optional Consent for Data and Specimen Banking for Future Research

Dr. Rynders would like to keep some of the data, blood, and saliva samples that are taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about how meal timing affects metabolic health. The research that is done with your data and samples is not designed to specifically help you. It might help people who have obesity and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Rynders keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him know that you do not want Dr. Rynders to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Rynders decides to destroy them.

When your data and samples are given to other researchers in the future, Dr. Rynders will not give them your name, address, phone number or any other information that will let the researchers know who you are.

Sometimes data and samples are used for genetic research (about diseases that are passed on in families). Even if your data and samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your data and samples include learning more about what causes obesity and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. Rynders will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by Dr. Rynders.

Please read each sentence below and think about your choice. After reading each sentence, circle “yes” or “no.” If you have questions, please talk to your doctor or nurse.

Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data, blood, and saliva samples to be stored in a central bank at the University of Colorado, Anschutz Medical Campus for future use by the study investigators:

1. I give my permissions for my data, blood, and saliva samples to be kept by Dr. Rynders for use in future research to learn more about how to prevent, detect, or treat obesity.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my data, blood, and saliva samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   ☐ Yes ☐ No _____Initials

3. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Corey Rynders, PhD,
UC Denver,
12631 E. 17th Ave., Mail Stop B179,
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- The National Institutes of Health which is paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

A description of this clinical trial will be available on http://www.Clinical Trials.gov. 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.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to

- Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Psychological and mental health tests
- Alcoholism, Alcohol, or Drug abuse
- Blood samples and the data with the samples

What happens to Data and Specimens that are collected in this study?

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data and blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data and blood sample given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data and blood collected from you.
- If data and blood specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures –
In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____