Study Title: Daily Caloric Restriction and Intermittent Fasting in Overweight and Obese Adults with Autosomal Dominant Polycystic Kidney Disease.

NCT03342742

Informed Consent Form

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Principal Investigator: Kristen Nowak, Ph.D., MPH
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Study Title: Daily Caloric Restriction and Intermittent Fasting in Overweight and Obese Adults with Autosomal Dominant Polycystic Kidney Disease.

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 weight loss in individuals with autosomal dominant polycystic kidney disease (ADPKD) who are overweight or obese. We will compare two different approaches to weight loss. One group will restrict the amount of calories they eat each day by about 34%. The other group will alternate each day between eating unrestricted and eating a very low calorie intake.

We want to study how feasible these two weight loss diets are in people with ADPKD. Both groups will participate in a group-based, weekly behavioral weight loss intervention weekly for 1 year. We will measure how will you adhere to and tolerate the diet and how much weight you lose. We will also look at changes in markers in your blood and the size of your kidneys by MRI. The results of this study will help us design a larger study where we can test if weight loss slows progression of ADPKD.

You are being asked to participate in this research study because you have ADPKD and are overweight or obese.

Other people in this study

Up to 40 people from your area will participate in the study.

What happens if I join this study?

If you join the study you will do the following:

Screening:

Your first study visit is called the screening visit. After signing this form, we will ask questions to determine if you qualify for the study. We will review your medical history, medications, and lab work. We may draw some blood from a vein in your arm if you do not have current lab work available. You will also have a short physical exam.

If you qualify for the study and agree to join the following will happen: You will be asked to participate for approximately a 1 year study (3 month intensive phase and 9 month maintenance phase) that will involve 1-2 visits to the testing clinic (these can be combined if you are traveling from outside the greater Denver metropolitan area) both at the beginning of the study and after 1 year. The diet period may be extended by several months during extenuating circumstances

limiting the ability to return the University of Colorado Anschutz Medical campus (e.g., COVID-19 outbreak).

Participation will take place in the research space of the Division of Renal Diseases and Hypertension Clinical Research Unit, the Anschutz Health and Wellness Center, and the Brain Imaging Center on the University of Colorado Anschutz Medical campus. The weight loss intervention will be conducted online through a secure website that will allow you to video chat with your instructor and other study participants.

You will be required to refrain from food (water is ok) prior to some of the visits. The study coordinator will review these restrictions with you.

If you live out of state, the lab work for screening and in the middle of the study may be arranged to occur elsewhere, and you will only need to come to the Anschutz Medical campus at the beginning and end of the study (1 year later). We may also need to review your medical records prior to your first visit.

Randomization:

This study will have 2 different groups of research subjects like you. To decide which group you will be in, we will use a method of chance. This method is like flipping a coin or rolling dice. Each group will get slightly different care. One group will participate in a weight loss program based on daily caloric restriction (DCR; eating about 34% less each day). The other group will alternate each day between eating unrestricted and eating a very low calorie intake (intermittent fasting (IMF). In both groups, the behavioral intervention will be delivered in a group setting online and taught by a registered dietitian with approximately 12-15 people randomized to the same treatment group as you.

Because of the design of the study, you will know which treatment group you are in, but your study doctor will not. This information needs to be kept secret from the study doctor so that the study is based on scientific results, not on peoples' opinions. During the 1 year that you are enrolled in the study, you will be asked not to participate in any other weight loss programs.

Table of detailed visits:

The table below illustrates the detailed visits if you enroll in the study.

	Visit 1 (Screening)	**Visit 2** (Baseline testing)	**Visits 3-26** (Weight loss intervention)	**Visit 27** (End of study visit)
Medical History	✖			
Physical Examination	✖			
Urine Sample	✖		✖ (only at month 3)	✖

Blood Draw	✖	✖	✖ (only at month 3)	✖
3-day diet record		✖	✖ (only at month 1 and 3)	✖
Questionnaires		✖	✖ (varies by visit)	✖
Vital signs and body measurements		✖	✖	✖
Resting energy expenditure		✖		
MRI for total kidney volume		✖		✖
Weight loss group meetings (online)			✖	

Explanation of each session:

Visit 1 (about 1 hr) (Screening):

- Medical History and Physical Examination. Your medical history and physical examination will be performed by a physician or nurse practitioner at the Division of Renal Diseases and Hypertension Clinical Research Unit. You will also be asked about your family history of kidney disease, cardiovascular disease, diabetes, and cancer. Your height, weight, waist circumference, and blood pressure will be measured. We will measure your heart rate and rhythm with an electrocardiogram (ECG).
- Blood Draw. A nurse or certified medical technician will place a small tube in a vein in your arm for drawing blood and will collect a blood sample (about 1 tablespoon) for routine blood tests and to evaluate study eligibility.
- Urine Sample. We will measure protein and creatinine in your urine.
- Pregnancy Test. If you are a female of reproductive age, we will perform a pregnancy test even if you are sure you are not pregnant. You cannot be in this study if you are pregnant.

Visit 2 (about 4 hrs) (Study Participation):

- Blood Draw. A nurse or certified medical technician will place a small tube in a vein in your arm for drawing blood and will collect a blood sample (about 1 ½ tablespoons) to measure markers related to reduced food intake.

- 3 Day Diet Record. You will be asked to complete a record in which you record all of your food and beverage intake for 3 days.
- Questionnaires. You will be asked to fill out questionnaires that give us information about your quality of life, mood, eating attitudes, and physical activity. You do not have to answer any questions that you do not want to answer.
- Weight and Vital Signs. Your height, weight, waist and hip circumference, blood pressure, and heart rate will be measured.
- Resting Energy Expenditure**.** We will measure the number of calories your body uses at rest by having you lie quietly for about 30-40 minutes, followed by a clear Plexiglas hood placed over your head for about 15-20 minutes. The hood will measure the air you breathe to determine the amount of oxygen and carbon dioxide. The entire test will take about 1 hour.
- MRI scan: You will have an MRI scan of your kidneys to measure the kidney size.

Visits 3-26 (about 1 ½ hrs):

- Weight Loss Group Meetings. You will be asked to virtually attend (online) weight loss group meetings on a secure website with about 12-15 other people in the study. Randomized groups (IMF and DCR) will meet separately. Each group will meet on a regular schedule weekly. Meetings will last about 60-90 minutes. They will occur weekly for the first 3 months of the study and then either monthly or twice a month for the remaining 9 months. If the diet period is extended by several months during extenuating circumstances limiting the ability to return the University of Colorado Anschutz Medical campus (e.g., COVID-19 outbreak), virtual group meetings will continue to be offered. Group meetings will be taught by a registered dietitian and will focus on making changes in your diet and eating behaviors to help you lose weight. There will be a mix of lecture presentations, individual worksheets, and discussion during the group meetings. You will be asked to keep a food log to help you monitor your food intake. You will be asked to weigh yourself on a scale at home prior to each group meeting and this information will be sent electronically to the study team. Group meeting attendance and completion of food logs will be tracked to monitor your progress in the weight loss program. You will also be asked to complete monthly surveys about your diet.
- Dietary Intervention. Both groups will reduce their overall calorie intake each week by the same amount (approximately 34%) for the duration of the 1 year study; however, study groups will use different eating patterns to reduce their weekly calorie intake:
    - **If you are randomized to the IMF group, you will be asked to perform a modified fast (eat only 20% of you energy needs) three days a week.** You will be provided will a calorie goal and sample menus to help you meet this modified fast day calorie goal. For most people, the calorie goal will be between 500-600 calories on the modified fast days. On non-fast days, you will be asked to eat a sensible, healthy diet, but you will not have to restrict your calorie intake.
    - **If you are randomized to the DCR group, you will be asked to eat about 66% of your energy needs every day for the duration of the study.** You will be given a daily calorie goal and sample menus to help you meet this goal.

- Blood Pressure. You will be provided with a home blood pressure monitor and asked to take your blood pressure monthly.
- 3 Day Diet Record and Questionnaires. Will be repeated at month 1 (visit 7) and month 3 (visit 16).
- Blood Draw and Urine Sample. Will be repeated at month 3 (visit 16) at a locally contracted laboratory (2 ½ tablespoons of blood).

Visit 27 (about 2 hrs):

- Blood Draw (about 2 ½ tablespoons) and Urine Sample
    - If you cannot return the University of Colorado at the 12 month time point, we will ask you to go to a locally contracted laboratory at this time for your clinical labs, and then remaining blood with be drawn at your end-of-study visit.
- 3 Day Diet Record
- Questionnaires
- Weight and Vital Signs
- ECG
- MRI

An additional blood draw(s) may be required if there are safety concerns or unexpected lab errors.

What are the possible discomforts or risks?

1. Risks of Weight Loss Program: You will be asked to decrease your calorie intake through DCR or IMF to help you lose weight and maintain your weight loss.

- *Common side effects*: The most common side effects associated with dietary weight loss interventions (both DCR and IMF) are likely to be hunger, fatigue, trouble sleeping, irritability, anxiety, headaches, impaired concentration, and cold intolerance. It is possible you may miss school or work, have to take medications, or have to see a doctor if you experience one of these diet related conditions.
- *Uncommon side effects*: Occasionally people can experience constipation, nausea, abdominal discomfort, or diarrhea when changing their usual diet. It is possible you could develop weakness, dizziness, lightheadedness, tremor, psychological stress or changes in your ability to think or process information when limiting your calorie intake. These conditions usually improve within a few weeks. Very rarely participation in a weight loss program can worsen an underlying eating disorder like anorexia, bulimia, or binge eating disorder. Very rarely, participation in a weight loss program can cause ongoing stress in relationships with friends, family and co-workers. Very rarely, participation in a weight loss program can impact performance or impair ability to function at home, school, or at work.

- *Rare and serious*: The most serious but rare side effect of reducing your calorie intake is gallstone formation, which usually only occurs with extremely low-fat diets. Very rarely dehydration, hypoglycemia (low blood sugar), electrolyte abnormalities, confusion, changes in mood or behavior, changes in ECG, arrhythmias (irregular heart rhythms), syncope (passing out), or seizures can occur with fasting or significantly limiting energy intake.

2. Risks of having an MRI: In this study we will take an MRI of your kidneys. The MRI machine uses powerful magnetic waves to take pictures inside the body. The waves themselves are not harmful, but they can cause metal to heat up and electronics to stop working.

You should NOT have an MRI if you have metal or electronic devices inside your body. Heart pacemakers and insulin pumps are examples of electronic devices.

The MRI machine is a small round tube. It might make you uncomfortable if you do not like tight spaces.

The most common side effect of having an MRI is flashing lights in the eyes. This is caused by the magnetic waves and is not harmful. Some people also experience warmth and reddening of the skin. This usually goes away after a few minutes.

If you are pregnant, be sure to tell the person giving you the MRI.

3. Risks of Having Blood Taken: During the entire study, a total of about 7 ½ tablespoons will be drawn. An additional 3 tablespoons (1 tablespoon at baseline, 1 at 3 months, and 1 tablespoon at the end of the study) if you sign the optional consent for future research. Up to an addition 1 ½ tablespoons may be required if an additional blood draw is needed. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube.

- *Common side effects*: 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.
- *Rare side effects*: There is also a small chance that you could feel lightheaded or faint during the blood draw.

4. Risks of Resting Energy Expenditure (REE): You may feel claustrophobic during the measurement of REE. You will have the opportunity to try the hood prior to beginning the measurement.

5. Risks if pregnant or become pregnant: If you become pregnant, the particular treatment or procedures involved in the study may involve risks to the embryo or fetus which are currently unclear. You may not be in the study if you are breastfeeding, pregnant, or plan to become pregnant during the study.

6. Group Behavioral Meetings: Due to the nature of the group setting to deliver the intervention, there is a risk of loss of privacy and confidentiality, including external knowledge of diagnosis of ADPKD and participation in a research study. You will be asked to keep confidential all identities and issues discussed during these group meetings.

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 can not be guaranteed.

The study may 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 eating patterns and weight in people with ADPKD. The study is not designed to treat any illness or to improve your health. Also, there could be risks to being in this study. If there are risks, these are described in the section describing the discomforts or risks.

Are there alternative treatments?

There may be other ways of treating ADPKD. Tolvapatan was recently approved by the FDA for individuals with rapidly progressing ADPKD. Other ways include lowering blood pressure if it is elevated. These treatments will be continued throughout the period of the study if you are already receiving them, and may be started at the beginning of the study period if you are not.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

The research is being paid for by the National Institutes of Health (NIH).

Will I be paid for being in the study?

You will not be paid for the completion of screening procedures or baseline measurements. You will be paid $25 for the diet record and weight at month 1 and $75 for the diet record, weight, blood draw, and questionnaires month 3 and month 12. This will add up to a total of $175 if you complete all of the visits. You will be paid $50 for any additional trips to the contract lab that may be required. Travel and hotel reimbursement may be offered if you do not live in the greater Denver metropolitan area.

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.

If you decide to leave the study early, you will be asked to make one final visit to the clinic to get a weight.

Can I be removed from this study?

You may be taken out of the study if the study doctor thinks it is not safe for you to be in the study. You will be removed from the study if you choose to participate in another weight loss program, research study, or if you chose to take a weight loss medication or supplement. You may be removed from the study if you do not regularly attend the group weight loss meetings. You can be taken out of the study even if you do not want to leave the study. Also, the sponsor can decide to stop the study at any time.

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. Nowak immediately. Her phone number is 303-724-4842. 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 Dr. Kristen Nowak. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Nowak at 303-724-4842. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Nowak with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

Optional Consent for Blood and Urine Banking for Future Research

Dr. Kristen Nowak would like to keep some of the blood and urine that are taken during the study but is not used for other tests. If you agree, we will keep some of the blood and urine already taken in the study and also take an additional tablespoon of blood at month 3 and month 12. If you agree, the blood and urine will be kept and may be used in future research to learn more about ADPKD. The research that is done with your blood and urine is not designed to specifically help you. It might help people who have ADPKD and other diseases in the future. Reports about research done with your blood and urine will not be given to you or your doctor. These reports will not be put in your health records. The research using your blood and urine will not affect your care.

The choice to let Dr. Kristen Nowak keep the blood and urine 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 blood and urine can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want Dr. Kristen Nowak to use your blood and urine any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Kristen Nowak decides to destroy them.

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

Sometimes blood and urine are used for genetic research (about diseases that are passed on in families). Even if your blood and urine 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 blood and urine will only be used for research and will not be sold. The research done with your blood and urine 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 blood and urine include learning more about what causes ADPKD 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. Kristen Nowak 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. Kristen Nowak.

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 blood and urine, you may still take part in the study.

I give my permission for my blood and urine to be stored in a central tissue bank at the University of Colorado for future use by the study investigators:

1. I give my permissions for my blood and urine to be kept by Dr. Kristen Nowak for use in future research to learn more about how to prevent, detect, or treat autosomal dominant polycystic kidney disease.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my blood and urine 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.

Dr. Kristen Nowak
Division of Renal Diseases and Hypertension
12700 East 19th Avenue, C281
Aurora, CO 80045
303-724-4842

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 (NIH), which is the entity 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.

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.)
- Your social security number

- Portions of my previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory studies, procedure results
- Research Visit and Research Test records
- Psychological and mental health tests

What happens to Data, Blood 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, 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, tissue, blood, or other specimens 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, blood, or other specimens collected from you.
- If data, blood, or other 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.

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.

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 _____