FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

INFORMED CONSENT DOCUMENT

Project Title: **Curcumin Supplementation for Improving Vascular and Cognitive Function in Chronic Kidney Disease**

Principal Investigator: Dr. Diana Jalal
University of Iowa
200 Hawkins Drive
Iowa City, Iowa 52242

Research Team Contact: Katie Geasland (319) 319-353-6318 or (319) 356-1616 pager #9971.

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have chronic kidney disease (CKD).

The purpose of this research study is to test an experimental drug called Curcumin.

An experimental drug is also "investigational." This means the drug has not been approved by the U.S. Food and Drug Administration (FDA).

In this study, the safety of Curcumin, its effects on the function of your blood vessels, and how well people tolerate it will be looked at. It will be compared to placebo. The placebo will look just like Curcumin, but has no medication in it. Both Curcumin and the placebo will be called "study drugs."

This study plans to learn more about the effects of curcumin on blood vessel function in middle-aged and older adults with chronic kidney disease (CKD). Curcumin is a dietary supplement and is a naturally occurring substance found in the Indian spice turmeric. Turmeric is commonly found in curry powder. You are invited to participate in this research study to determine whether curcumin can improve the function of your blood vessels.

Function of blood vessels is affected by how stiff they are and by a layer of cells called the endothelium. In kidney disease the blood vessels do not function properly. The reason they do not function properly is not known.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

Patients with CKD are at a higher risk for cognitive impairment. Therefore, we will also assess if curcumin can improve your cognitive function.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 120 people will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 52 weeks and will have 5- 7 in person study visits. The time you will spend at each clinic visit will range from 30 minutes to 5 hours depending on the visit. The approximate time needed for each clinic visit is listed in the "WHAT WILL HAPPEN DURING THIS STUDY" section below.

WHAT WILL HAPPEN DURING THIS STUDY?

Screening:

If you agree to take part in this study, you will be asked to undergo an initial set of tests aimed at establishing your general health status and overall eligibility to participate in the study.

Randomization:

This study will have 2 different groups of research participants 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 case. One group will receive curcumin and the other will receive a placebo. A placebo is a pill or a liquid that looks like medicine but is not real. It will have no medical effect on you. In both groups, the drug or placebo will be given to you as a pill.

You will not know which treatment group you are in, nor will the person running the study, or your doctor. This information needs to be kept secret so that the study is based on scientific results, not on people's opinions. However, we can give this information out if you have an emergency. If you are in an emergency, make sure you tell the emergency staff about this study. They can contact us, and we will give them all relevant information.

After the study is over, the study team will find out which participants have been given study drug or placebo (this process is called un-blinding). The study team will also review the study and do an initial review of all the study data that was collected. The study team will send you a letter that contains an overview of these preliminary results and they will also tell you if you were receiving study drug or placebo. This letter will be sent to the address we have on file for you.

Dosing of medication:

If you are randomized to the study drug, you will take 2,000mg/day of the study drug via pill. If you are in the placebo group you will still receive pills, but the placebo pills will not contain any active ingredients.

It is important for you to follow the instructions of the study team regarding how to take your study drug. You will be asked to bring any unused study drug and your empty pill bottles with you to every

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

study visit.

The table below illustrates the detailed visits if you enroll in the study. **Table of detailed visits:**

	Screening visit	**Baseline visit**	**Month 1 & 3 visits**	**Month 6 visit**	**Month 9 visit**	**Month 12 visit**
Medical history & physical exam, including skin-fold calipers	**X** (may be completed at baseline visit)	**X** (if not completed at screening visit)				
Blood draw	**X** (if needed)	**X**		**X**		**X**
Urine sample	**X** (if pregnancy test is needed)	**X**	X (if pregnancy test is needed)	**X**	X (if pregnancy test is needed)	**X**
Resting blood pressure	X	**X**		**X**		**X**
IV and endothelial cell collection		**X**		**X**		**X**
Blood vessel stiffness and endothelial function tests		**X**		**X**		**X**
Saline and vitamin C infusions		**X**		**X**		**X**
Nitroglycerin		**X**		**X**		**X**
Cognitive testing/surveys		**X**				**X**
Receive study drug		**X**	X (3 month only)	X	X	
Pill count			**X**	**X**	**X**	**X**
Adverse event questionnaire			**X**	**X**	**X**	**X**
Physical activity questionnaire	**X**			**X**		**X**

Explanation of each visit:

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

Screening visit (about 1.5 hours):

- Medical history and physical exam: Your medical history and a physical examination will be performed by a physician or nurse practitioner at the Clinical Translational Research Center (CTRC). You will also be asked about your current medications as well as your family history of kidney disease, cardiovascular disease, diabetes, and cancer. Your body weight and height will be measured using a doctor's office scale.
- Blood pressure at rest: Your blood pressure will be measured after resting using a cuff on your upper arm.
- 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 5 teaspoons) to measure markers of kidney and liver function (if these levels have not been measured in the last 6 months)
- Pregnancy test: If you are a female of possible child-bearing age, a urine pregnancy test may be required.
- Physical activity questionnaire
- Lean body mass assessment: Using skin-fold calipers, a member of the study team will take measurements on three parts of your body.

Baseline visit (about 5 hours):

- Blood pressure at rest: Your blood pressure will be measured after resting using a cuff on your upper arm.
- Urine sample: We will collect a sample of urine to measure markers of kidney function.
- Pregnancy test: If you are a female of possible child-bearing age, a urine pregnancy test may be required.
- An IV catheter will be placed in one of your arms by a CRU nurse, a study physician or a properly trained member of the research team. The catheter will be used to during the endothelial cell collection, blood draw and the saline and Vitamin C infusion.
- Endothelial cell collection: A nurse will place up to three very small (0.021 inch diameter) J-shaped wires inside the IV in your arm. The wire will immediately be pulled out and will contain some cells from the inside of your vein (endothelial cells).
- 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 to measure markers such as kidney and liver function, inflammation, and cholesterol.
- You will be given a snack after the blood draw.
- Cognitive testing (*Approximately 45 minutes*): You will complete tests on a computer tablet to assess your attention, memory, language, executive function, and processing speed.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

- **Attention (Approximately 3 minutes):** Attention is the foundation for all mental processes. It refers to your ability to manage the abundance of environmental stimulation and is measured by the NIH Toolbox Flanker Inhibitory Control and Attention Test. During this test you will be required to focus on a given stimulus while inhibiting attention to another stimulus.
- **Episodic Memory (Approximately 7 minutes):** Episodic memory refers to processes involved in the acquisition, storage, and retrieval of new information and is measured by the NIH Toolbox Sequence Memory Test. You will be shown a series of objects and activities in a particular order on the screen. You will be asked to recall the sequence of the pictures.
- **Working memory (Approximately 7 minutes):** Working memory refers to your ability to store information until your storage capacity becomes overloaded and is measured by the NIH Toolbox List Sorting Working Memory Test. You will be shown different pictures of foods and animals with accompanying audio and written text and will be asked to say the items back in size order from smallest to largest.
- **Language (Approximately 7 minutes):** Language refers to your ability to translate thought into words and gestures that can be shared among individuals for communication. This study will focus on two aspects of language: vocabulary knowledge (measured by the NIH Toolbox Picture Vocabulary Test) and oral reading skill (measured by the NIH Toolbox Oral Reading Recognition Test). You will be presented with an audio recording of a word and four photographic images on the computer screen and will be asked to select the picture that most closely matches the meaning of the word. You will also be asked to read and pronounce letters and words as accurately as possible.
- **Executive function (Approximately 4 minutes):** Executive function is your ability to plan, organize, and monitor behaviors that are directed towards a specific goal and is measured by the NIH Toolbox Dimensional Change Card Sort Test (DCCS). You will be shown two pictures that vary by shaped and color and will be asked to match a series of pictures by shape and then by color.
- **Processing speed (Approximately 3 minutes):** Processing speed is the amount of time it takes you to process a set amount of information and is measured by the NIH Toolbox Pattern Comparison Processing Speed Test. You will be shown two pictures side-by-side and will be asked to determine whether they are the same or not.
- **Immediate recall (Approximately 3 minutes):** Immediate recall refers to your ability to immediately recall information. You will be asked to recall unrelated words that are presented by audio recording. This is measured by the NIH Toolbox Auditory Verbal Learning Test.
- **Processing speed (Approximately 3 minutes):** Processing speed is the amount of time it takes you to process a set amount of information and is measured by the NIH Toolbox Oral Symbol Digit Test. You will be shown symbols associated with numbers. Then you will be shown symbols without numbers and will say each number that goes with the symbol.

You will also be asked to complete surveys regarding anxiety, depression, fatigue and pain.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

- Blood vessel stiffness test: To test the "stiffness" of the walls of your arteries we will do two sets of measures. First, a small probe will be placed flat on the surface of your skin at four sites and will record each time your heart beats. The four sites are your carotid artery (side of neck), brachial artery (near the back of your elbow), femoral artery (upper leg/hip), and radial artery (wrist). The faster your pulse moves between the sites, the stiffer your arteries are. Second, an ultrasound will also be used on the surface of your skin to allow us to see how the size of an artery on the side of your neck (carotid artery) changes at rest. This tells us how elastic (the opposite of stiffness) your artery is.
- Endothelial function test: We will place an ultrasound probe on your skin over the major artery in your upper arm. A small blood pressure cuff will be inflated tightly below your elbow cutting off the blood flow for 5 minutes. The blood flow and size of your vessel will be measured before and after inflating the cuff. This will allow us to measure your endothelial function (ability of blood vessels to dilate or get bigger). You will also have electrodes on your chest to trace the electrical activity of your heart (ECG).
- Nitroglycerin: A nitroglycerin pill will be placed under your tongue. Nitroglycerin is given to patients to relieve chest pain. This pill will cause the major artery above your elbow to increase in size. We will look at your blood pressure and will collect ultrasound images of your blood vessel for 8 minutes after you take the nitroglycerin pill.
- Endothelial function test is repeated

- Saline infusion: We will infuse saline (water with salt) into the IV in your arm for about 30-60 minutes. After 20 minutes of the infusion, we will repeat the measurements of blood vessel function described above (Endothelial function test).

- Vitamin C infusion. We will then infuse vitamin C into the IV in your arm/hand for about 30-60 minutes. After 20 minutes of the infusion, we will repeat the measurements of blood vessel function described above (Endothelial function test).
- Remove your IV and offer you a meal, if you would like one.
- Receive study medication: A study staff member will give you study drug to take at home. You will be given a three month supply of the study drug at this visit. You will be instructed to take one dose (total of 4 pills) of the study drug per day. You will also be asked to bring your supply back to each visit so that we can count how many study drug pills you have taken since your last visit.

Month 1, 3, and 9 (about 0.5 hrs):

- Pill count: A member of the study team will count how many study drug (active or placebo) pills you have taken since your last study visit.
- Adverse event questionnaire: You will complete a questionnaire to assess if you have experienced any side effects or any adverse events since your last study visit.
- Pregnancy test: If you are a female of possible child-bearing age, a urine pregnancy test may be

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

required.

- Month 1 visit may be in the form of a phone call with you providing a count of the number of pills taken and providing answers to adverse event questionnaire.

- At your 3 and 9 month visits, you will receive another 3 month supply of study medication.

- If you are unable to make an in-person visit, a safety visit via phone will be made and the study medication will be mailed out.

Month 6 visit (about 4 hours):

The following procedures will be done and are described in the Baseline visit section:

- Blood pressure at rest
- Urine collection
- Pregnancy test: if you are a female of possible child-bearing age
- Endothelial cell collection
- Blood draw
- Snack
- Blood vessel stiffness test
- Endothelial function test
- Nitroglycerin (with endothelial testing repeated)
- Saline infusion (with endothelial testing repeated)
- Vitamin C infusion (with endothelial testing repeated)
- IV removed and a meal will be offered, if you want one.
- You will receive another 3 month supply of study medication. If you are unable to keep this scheduled appointment, due to unanticipated circumstances, additional study medication may be mailed out to carry you over until you can be scheduled for an in-person study visit.

Additionally, you will complete the following questionnaires:

- Adverse event questionnaire
- Physical activity questionnaire
- Study drug pill count

Month 12 visit (about 5 hours):

The following procedures will be done and are described in the Baseline visit section:

- Blood pressure at rest
- Urine collection
- Pregnancy test: if you are a female of possible child-bearing age
- Endothelial cell collection
- Blood draw
- Snack

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

- Cognitive testing and surveys
- Blood vessel stiffness test
- Endothelial function test
- Nitroglycerin (with endothelial testing repeated)
- Saline infusion (with endothelial testing repeated)
- Vitamin C infusion (with endothelial testing repeated)
- IV removed and a meal will be offered, if you want one.
- If you are unable to keep this scheduled appointment, due to unanticipated circumstances, additional study medication may be mailed out to carry you over until you can be scheduled for an in-person study visit.

Additionally, you will complete the following questionnaires:

- Adverse event questionnaire
- Physical activity questionnaire
- Study drug pill count

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

The data, tissue, 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, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, researchers 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.

Some of the blood and urine samples will be processed in the University of Iowa Hospitals and Clinics lab. These tests will evaluate your health, kidney and liver function. You will be given the results of these tests and those results will also be available in your Epic medical record for any of your treating physicians at the University of Iowa Hospitals and Clinics to see now and in the future.

Tissue/Blood/Data Storage for Future Use

Optional Consent for Blood, Urine, and Endothelial Cell Banking for Future Research

The study investigators would like to keep some of the data, blood and urine that is 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

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

future research to learn more about chronic kidney disease. The research that is done with your data and samples is not designed to specifically help you. It might help people who have chronic kidney disease 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 the study investigators 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 or her know that you do not want the study investigators 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 the study investigators decides to destroy them.

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

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.

Your sample, information, and/or data may be placed in a central repository or other national repositories sponsored by the National Institutes of Health or other Federal agencies. If so, it will be stripped of identifiers (such as name, date of birth, address, etc.). Other qualified researchers who obtain proper permission may gain access to your sample and/or data for use in approved research studies that may or may not be related to in the purpose of this study.

The possible benefits of research from your data and samples include learning more about what causes chronic kidney disease and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. The study investigators 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 the study investigators.

Please read each sentence below and think about your choice. After reading each sentence, mark "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 urine to be stored for future use by the study investigators:

1. I give my permissions for my data, blood and urine samples to be kept by the study investigators for use in future research to learn more about how to prevent, detect, or treat chronic kidney disease.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

☐ Yes ☐ No _____Initials

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

☐ Yes ☐ No _____Initials

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

☐ Yes ☐ No _____Initials

WILL YOU KEEP MY NAME ON FILE TO GIVE TO OTHERS?

We may keep information about you in a special kind of computer listing called a registry. A registry keeps information about you on file so that *other* researchers, not involved in this particular study, may contact you in the future about whether you are interested in being in *different* research studies. The registry will contain information such as your name, contact information, age, and CKD medical history.

We may share the information in this registry with other researchers at the University of Iowa. We will keep the information in this registry secure by maintaining a secure, password protected database that only certain members of the research team have access to. If you first agree to be added to this registry but then change your mind, you may request that your personal information be removed from this file at any time by contacting: Dr. Diana Jalal at (319) 356-3971.

Having your name on this registry is optional. If you do not want your name added to the registry, you may still participate in this study.

Do you give us permission to add your name and personal information to a registry so that other researchers at the University of Iowa can contact you in the future about different research studies?

☐ Yes ☐ No _____Initials

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Discomforts you may experience while in this study include:

1. Risk of receiving curcumin: Curcumin is a dietary supplement that is the active ingredient in the Indian spice turmeric. It is designated as "generally recognized as safe" by the FDA. Few side effects of curcumin have been reported, and this was primarily with higher doses than will be given in this study. The primary risk is possible gastrointestinal distress (gas, constipation, diarrhea, or nausea) in a small

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

percentage of people. Rarely, curcumin may cause dizziness. In the event that you develop symptoms that are not tolerable, we will reduce your dose of curcumin.

2. Risk of receiving nitroglycerin under the tongue: Nitroglycerin is a drug used medically to treat chest pain.
   Common side effects: The most common reaction to this medication is a headache which develops in approximately 60% of patients.
   Less common side effects: It can also cause a decrease in blood pressure, dizziness or lightheadedness. The fall in blood pressure mainly occurs when the person is standing or sitting upright and in this study you will receive nitroglycerin while lying on your back. Placing the pill under your tongue may cause irritation in that area of your mouth.
   Rare side effects: In rare instances (1 in 1000) it may lower the heart rate, which could cause fainting. Fainting mainly occurs when the person is standing or sitting upright and in this study you will receive nitroglycerin while lying on your back.
   These risks will be minimized by carefully monitoring your blood pressure and heart rate every 2 minutes following administration of nitroglycerin. In addition, you will have an IV in place so fluids can be given if your blood pressure falls or fainting occurs.

If you are allergic to, or have had an adverse event after taking, any of the above drugs, please notify the investigator before participating.

3. Risks of having blood taken: In this study we will need to collect a total of about ¾-1 cup of blood from you. 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. Risk of having an IV inserted in your vein: In this study, we will insert a needle, connected to a plastic tube, into a vein in your arm. We will use the tube to take blood samples or give you fluids.
   Common side effects: You will feel some pain when we first insert the tube into your vein. You may have some redness, swelling or bruising where the tube goes under your skin.
   Rare side effects: There is a small chance that you could feel lightheaded or faint during the IV insertion. In some cases, this type of tube can cause an infection where it goes under the skin, but the risk of infection is less than 1 in 1000. In rare cases, it can cause a blood clot in the vein.

5. Risk of endothelial cell collection:
   Common side effects: The risks related to the endothelial cell collection are similar to those of an IV, including some pain and possibly some redness, swelling, or bruising.
   Rare side effects: The risk of blood clots and infection may be slightly greater than those of an intravenous catheter due to increased manipulation of the blood vessel when compared with catheterization alone. There is also a very low likelihood that the J-shaped wire could get stuck in the vein and/or that the vein could be damaged.

6. Risk of vitamin C infusion:

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

Rare side effects: There is a chance the vitamin C may irritate your skin on your hand where it is being infused, but this uncommon because we dilute (water-down) the vitamin C in saline (water with salt).

7. Risk of endothelial function test:
   Common side effects: Inflating the blood pressure cuff just below your elbow during this test may cause a moderate intensity pain "pins and needles" or numbing sensation that goes away as soon as the cuff is deflated.

8. Risks if pregnant or become pregnant: You may not be in the study if you are breastfeeding, pregnant, or plan to become pregnant during the study. Discuss with your doctor acceptable birth control methods. There are no known risks of curcumin during pregnancy to mother or child. If you become pregnant while taking part in the study, you must immediately tell your research doctor. Options will be discussed with you at that time. Whether or not you remain on study treatment, we will follow the outcome of your pregnancy and we will continue to follow you according to the study plan. You will be given a urine pregnancy test prior to receiving any of the study medications.

9. Stress as a result of cognitive testing: You may experience stress as a result of undergoing the cognitive testing.

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 include risks that are unknown at this time.

WHAT ARE THE BENEFITS OF THIS STUDY?
We don't know if you will benefit from being in this study. This study is designed for the researcher to learn more about the effects of curcumin on blood vessel and cognitive function in adults with CKD.

WHAT OTHER TREATMENT OPTIONS ARE THERE?
There may be other ways of treating your CKD. These other ways include lowering blood pressure, in addition to lowering blood sugar, and cholesterol. You could also choose to get no treatment at all.

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.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?
You will not have any costs for being in this research study.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?
You will be paid for being in this research study.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

Baseline and 6 month visits: $100.00 for each visit
3 and 9 month visits: $25.00 for each visit
12 month visit: $150.00 for this visit

You will be given parking vouchers to cover the cost of parking in the UIHC parking ramp while you are completing your visits.

If you live outside the Iowa City and Coralville area, you will be paid for your mileage at $0.20 per mile.

This will add up to a total of $400.00 if you complete all of the visits. 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.

You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. Your social security number is obtained for payment purposes only, it will not be retained for research purposes.

WHO IS FUNDING THIS STUDY?

National Institutes of Health is funding this research study. This means that the University of Iowa is receiving payments from National Institutes of Health to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from National Institutes of Health for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Federal government regulatory agencies such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you and the National Institutes of Health
- The study doctor and the rest of the study team
- Auditing departments of the University of Iowa, and
- The University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

To help protect your confidentiality, we will store all the data we gather from you in locked files and in a secure database that can only be accessed by the study team. You will be assigned a unique study identification (ID) number and all of your data, tissue, blood, and specimens collected from you will be stored under this unique study ID. All electronic files are stored on password protected computers that are connected to a secured shared drive. The data entry for the study is completed using a database created in RedCap. All members of the team have an individual log-on and secure password.. . Your blood and urine samples that are being sent and processed in the University of Iowa Hospitals and Clinics lab will have your name and medical record number on them so that they may be processed and the results stored in your medical record (see What happens to Data, Tissue, Blood and Specimens that are collected in this study? section above). Only the Principal Investigator and the study team will have access to the RedCap database that links your name with your study ID. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, and the National Institutes of Health.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your health care provider to give us permission to use or create health information about you.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to:

Diana Jalal, M.D.
200 Hawkins Drive
Iowa City, Iowa 52242

However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

If you decide to leave the study early, you will be asked to make one final visit so that you can you can complete the testing planned for the final visit.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because, if in our judgment, it would not be safe for you to continue, because your condition has become worse, or because you are or became pregnant.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Dr. Diana Jalal at (319) 356-3971.

FOR IRB USE ONLY
APPROVED BY: IRB-01
IRB ID #: 201710769
APPROVAL DATE: 08/15/22
EXPIRATION DATE: 08/15/23

If you experience a research-related injury, please contact: Dr. Diana Jalal at (319) 356-3971.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 08/15/23.

_____ _____

(Signature of Subject) (Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____

(Signature of Person who Obtained Consent) (Date)