COVER PAGE FOR PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official Study Title: SGLT2 Inhibition in Older Obese Adults With Pre-diabetes

NCT number: NCT04401904

IRB Approval Date: 09-22-2021

Unique Protocol ID: HSC20190766H

Concise Summary

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled and will not affect your relationship with us.

1. What problem is this study trying to solve?
You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future**.** The purpose of the research study is to evaluate whether pre-diabetic older adults can benefit from taking a drug called dapagliflozin (Brand name FARXIGA) to reduce cellular damage, pro-inflammatory cells of aging also called "senescent cells", and other known markers of biological aging.

For more information, please see the *Why is this Study being Done* section below.

2. What will happen to me during the study and how is this different from continuing with usual care? What are all my options for treatment, including the pros and cons?
Eligible participants will undergo laboratory assessments of blood and urine, assessment of memory, and receive by random assignment either the study medication or nutritional counseling over a 12-week period. Participants complete pre- and post-treatment testing including: medical history, physical examination, physical performance measures like walk distance, handgrip strength and knee extensions, riding an exercise bike to measure oxygen consumption, and muscle and fat sampling. Other pre- and post- measures include a body composition scan (called a DEXA), a liver ultrasound scan, and magnetic resonance (MR) testing to evaluate fatty deposits in the liver.

For more information, please see the ***What will be done if you decide to be in the research*** section below.

3. How much time will I spend on the study?
This study involves 14 total visits (Visit 1,2,3,4,5,6,7,8,9,10,11,12) over the course of approximately 16-18 weeks. Visits are scheduled every 2-4 weeks and may last anywhere from 30 minutes to 3 hours depending on the procedures involved.

4. Could taking part in the study help me and are there risks?
We cannot guarantee that you will benefit from participating in this study other than to receive study medication and study related clinical care at no cost to you, and a small amount of reimbursement for your time and travel to the research unit.

The risks associated with your participation may include medication side effects, pain or bleeding from blood draws and muscle or fat samplings, emotional distress from assessments, or fatigue from physical performance measures.

For more information, please *see* ***How could you or others benefit from your taking part in this study*** section below. For details and a list of risks you should know about, please see the ***What are the risks of participation in the research*** section below.

5. What else should I consider before I make my decision?
This study will involve attending study visits at UT Health San Antonio (UTHSA) McDermott Clinical Sciences Building (MCD), the UTHSA Research Imaging Institute (RII at MCD) and the UTHSA Medical Arts & Research Center (MARC) at 8300 Floyd Curl Drive, and Barshop Institute Clinical Research Center (BICRC) 4939 Charles Katz Dr.

Please review the rest of this document for additional details about these topics and other information you should know before making a decision about participating in this research.

Title of Study: Effect of SGLT2 inhibition on aging-related biomarkers in older obese adults with pre-diabetes

Consent to be part of a Research Study
To be conducted at
University of Texas Health Science Center at San Antonio,

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the researchers or study staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are entitled.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety and welfare as a participant in the research. The PI for this study is Carolina Solis-Herrera, MD, Assistant Professor UTHSA Department of Medicine, Diabetes Division.

Funding
Non-Profit or Federal Agency Funding
The National Institute of Aging (NIH-NIA) Claude D. Pepper Older Americans Independence Center, a federal agency that promotes scientific research, is funding this study. This organization is providing money to UTHSA Sam and Ann Barshop Institute for Longevity and Aging Studies so that the researchers can conduct the study.

Purpose of this study – "Why is this study being done?"

The purpose of the research study is to evaluate whether pre-diabetic older adults can benefit from taking a drug called dapagliflozin (Brand name FARXIGA) to reduce cellular damage, pro-inflammatory cells of aging (senescent cells), and other known biological markers of aging.

You are asked to participate in this research study of pre-diabetes and aging, neither of which are known to have current medical treatment except for lifestyle and behavioral changes (diet, exercise, sleep).

The researchers hope to learn whether dapagliflozin can influence physical performance, biomarkers of aging, and delay the onset of diabetes if used in the pre-diabetic state.

Investigation Use of Drug
This study involves the use of an investigational drug called dapagliflozin (Brand name FARXIGA). "Investigational" means that the drug has not yet been approved by the U.S. Food & Drug Administration (FDA) for treating/preventing/diagnosing pre-diabetes and is approved for use in diabetes.

This study will help find out what effects, good and/or bad, this drug has on people who take it and its effect on aging and pre-diabetes. The safety of this drug in humans has been tested in prior research studies; however, some side effects may not yet be known.

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

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you are age 60 years or more and have pre-diabetes.

This study will enroll approximately 30 study participants.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 12 visits with the researchers or study staff. It may be necessary for you to return to the clinic every 2 to 4 weeks.

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will obtain and which procedures will not have to be repeated. You will be told which procedures are for "research only".

Screening Procedures (research only)
Participants will be asked to arrive in a fasting state to the research unit for vital signs and screening procedures. Please see Visit 1 for details.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you.

If screening lab test results are abnormal, the investigator will make a clinical decision whether to repeat the tests and when that should occur.

While taking part in this study, participants will spend at least 30 min-4 hours at each visit depending on procedures being done.

Assignment to Study Groups – happens at Visit 5 **(research only)**
When it is determined that you are eligible for the study, you will be assigned by chance (like flipping a coin to one of two study groups.

- Take the study drug (open label), dapagliflozin (Brand Name: FARXIGA) 10 milligrams by mouth for 12 weeks (study drug may be dispensed in person, during home visits, curbside delivery, or by U.S. mail), -or-
- Receive nutritional counseling and no study drug

Study Procedures

- Visits will be performed at the UT Health San Antonio Medical Arts and Research Center (MARC), or the Barshop Institute Clinical Research Center, except for magnetic resonance studies (MRI imaging) that will be done at the Research Imaging Institute. You will be asked to arrive fasting (10-12 h) for visits involving lab work, imaging, or biopsies.
- Please note that your participation in this study may involve remote and/or virtual research interactions with our research staff. You will be audio and/or video recorded using the conferencing platform, Zoom, for the remote visit. Therefore, privacy and confidentiality are not guaranteed due to the nature of the research environment.

- ❖ You will be given a Fitbit Bluetooth digital scale that will allow you to weigh yourself at home and submit your weight to the study staff electronically using the Fitbit app. Your scale will be connected to an email account that will be created and managed by the study staff and will only be used to collect the data from your scale. The study staff will help you install and setup the Fitbit app on your mobile device and connect your scale. If you do not have access to a mobile device or are unable to use the Fitbit app on your device, you will use the scale to take your weight and provide your documented weight to the study staff during home visits or by telephone. The scale will be provided to you free of charge.
- ❖ Visits that require DEXA scans and MRI scans may be performed in reverse order based on scheduling availability of the DEXA and MRI procedures.

Visit 1 – Screening (research only)
The screening procedures are for research purposes.

- ❖ Vital signs – typical assessments like blood pressure, heart rate, respiration rate, and temperature; may also include height and weight
- ❖ Medical history – a listing of your history of illnesses, surgeries, social habits, medications and allergies
- ❖ Physical examination – a general exam like what you would have in your primary physician's office
- ❖ Safety labs, a blood draw used to assess your general health status
  - complete blood count (CBC)
  - blood chemistry/comprehensive metabolic panel (CMP) and lipid panel (lipids)
  - coagulation tests (PT/PTT/INR) to assess how fast your blood will clot
  - hemoglobin A1c (HbA1c, a 3-month average reading of blood glucose levels)
  - insulin and FFA (free fatty acids)
  - thyroid stimulating hormone (TSH, an indicator of your thyroid function)
  - routine urinalysis (UA) to rule out urinary infection
- ❖ Montreal Cognitive Assessment (MoCA) an assessment of memory and thinking to ensure the understanding of study intent (purpose of the study) and the consent document

Your appointment for Visit 1 will take about 2.5 to 3 hours.

Visit 2 - Strength testing, Body composition (DEXA) and Liver Fibroscan (baseline) Research only**
Eligible participants will present to the MARC research unit to undergo the following:

- ❖ Vital signs
- ❖ Walk distance – to measure the distance you can walk over a period of 6 minutes
- ❖ Grip strength – using an instrument called a dynamometer that measures hand grip strength when you squeeze as hard as you can
- ❖ Isometric knee extension strength testing – to measure your leg strength, we will use a leg press machine like you would see in the gym
- ❖ DEXA scan – we will measure the total amount of fat and muscle in your body by a technique called Dual Energy X-ray Absorptiometry. During this procedure, which will last about 10 minutes, you will lie on an imaging table while an x-ray camera passes over your body from head to foot. The distance between the camera and your body will be about two feet. During the DEXA study, you will have to lie flat on your back. You will receive a small amount of radiation during the test. Other than this, there are no known risks associated with this exam.
- ❖ Liver fibroscan - we will perform a test that uses ultrasound to measure the amount of fibrosis (thickening or scarring of tissues) in your liver. It can be used alone or with other tests (such as biopsy, blood tests, ultrasounds) to see how much scarring there is on your liver. Fibroscanning is a pain-free diagnostic test that uses an ultrasound wand placed on your abdomen in the right upper quadrant where the liver is located using a lubricant gel to create a special image of your liver. The procedure usually takes about 5-10 minutes.

- Assessment of adverse events – we will ask you if you have had any (unexpected) medical experiences (events) since the last visit
- You will be given an appointment for imaging at Visit 3 and directions to the UT Health San Antonio Research Imaging Institute

Your appointment for Visit 2 will take about 2 hours.

Visit 3 – Magnetic Resonance Spectroscopy and Imaging (baseline) Research only**
You will be asked to go to the UT Health San Antonio Research Imaging Institute to undergo:

- Assessment of adverse events – we will ask you if you have had any (unexpected) medical experiences (events) since the last visit
- Magnetic Resonance spectroscopy (MRS) and Magnetic Resonance Imaging (MRI) of the liver - this exam will assess the intrahepatic liver fat (fatty tissue situated or occurring within or originating in the liver) that may be deposited there.
  - The MRS provides a non-invasive view of the biochemical processes within the body, in this case, the liver.
  - There is no radiation associated with this procedure. You will be required to remove any external metal objects (cell phone, watch, jewelry, etc.) from your person because the magnet is very strong.
  - If you have severe claustrophobia (fear of confined spaces, like a crowded elevator), have metal implants in your midsection or upper body, or have a pacemaker, you will (not have the procedure done).

Your appointment for Visit 3 will take about 1.5 hours.

** Visits 2 and 3 may be performed in reverse order based on scheduling availability of the DEXA and MRI scans.

Visit 4 -- Cardiopulmonary exercise testing (baseline) Research only -- {Optional}:
You will be asked to present to the BICRC for the following:

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- Cardiopulmonary (heart and lung) exercise testing (CPET/VO2max) – cycling on a stationary bike to determine how much oxygen your body requires during 10 minutes of endurance exercise. As part of this assessment, you will receive a 12-lead electrocardiogram (test which measures the electrical activity of your heart) (ECG) to monitor your heart rate and rhythm while you exercise while measuring the level of oxygen you require and carbon dioxide that is produced as a result.
  - This visit is optional. You may choose to not complete this visit by initialing below:

    _____ I do not wish to complete Visit 4 (heart and lung exercise testing and electrocardiogram)

Your appointment for Visit 4 will take about 1 hour.

Visit 5 – Muscle and Fat sampling (Day 0) Research only
You will be asked to present in a fasting state (no food or drink past a specified time the night before the exam) to the BICRC to undergo the following procedures.

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- Muscle biopsy
  - We will take 1-2small samples of your thigh muscle using a special needle. These are called muscle biopsies.

- To do this, we will clean your thigh and inject a local anesthetic (numbing medicine like your dentist uses) to numb a small area of your skin. We may have to shave a small area for the incision. We will clean the area with a special antiseptic solution. Next, we will make a small cut in your skin (about ¼ inch). The biopsy needle will then be passed through this cut into the muscle and a piece of muscle tissue about the size of a pea will be obtained. At the time the muscle is obtained, many people feel pressure and a thumping sensation. About a third of people feel cramping or pain. The pain is mild to moderate and lasts 5-10 seconds. The pain stops when the needle is removed but your muscle may be sore for a few days.
- In the areas where the biopsies were done, we will apply strips of adhesive tape (Steri-strips®) that will help the skin to close. The adhesive tape will come off on its own, and you do not need to peel it off.
- We will give you lunch and monitor how you feel until you are ready to go home.

❖ Fat biopsy
- We will take 1-2 small samples of fatty tissue about the size of a grape from the area on your belly below the navel level. This is called fat biopsy.
- To do this, we will clean an area on your belly below navel level and inject a local anesthetic (numbing medicine like the dentist uses) to numb the area first. We will clean the area with a surgical-grade antiseptic solution.
- Next, we will make a small cut in your skin (about ¼ inch) of the numb area to administer more numbing solution in a technique known as infiltration (spreading the numbing solution under the skin across an area about the size of the span of your fingers).
- Using an instrument that looks like a narrow straw (called a cannula) we will connect the instrument to the suction apparatus to collect tissue in a manner similar to a liposuction procedure.
- If the sample amount appears to be enough, we will apply a bandage and cover it for protection. We will instruct you how to care for the wound.
- If the sample appears to be not enough tissue from the “first pass”, and while the area is still numb, we may make a “second pass” with the straw-like instrument through the same incision to collect a little more tissue.
- After the procedure, we will give you lunch and monitor how you feel until you are ready to go home.

❖ Blood draw – similar to the blood draw at Visit 1, approximately 2 tablespoons will be drawn for research-only to analyze blood markers of inflammation that are thought to be related to aging

❖ Urine specimen – similar to a routine urine collection that will be analyzed for urine markers of inflammation related to aging

❖ Treatment assigned (randomization)
- You will be assigned to either the drug treatment group (dapagliflozin group) or to the nutritional counseling group (control group)
- If assigned to dapagliflozin you will be dispensed a 1-month supply of study medication with verbal instructions for administration
- If assigned to the control group, you will be weighed and scheduled for nutritional counseling. The nutritional counseling visit may be conducted by video, using your phone or computer.

After treatment begins, study staff will contact you by phone to follow up 1 week after Visit 5, and every 2 weeks between visits until Visit 8.

This visit will take approximately 2 to 2.5 hours.

Visit 6 – Biopsy check and treatment follow up (Week 4) Research Only

You will be asked to return to the BICRC research unit to have your biopsy site checked and for the procedures listed below. If necessary, you may be scheduled for a home visit or a remote video visit and may receive your medication in person, by mail or curbside delivery:

- Biopsy check – we will examine the area on the thigh where the biopsy procedure occurred
- Blood draw – CMP to monitor kidney function
- Treatment dispensing – based on your group assignment, you will receive either study medication with follow up instructions or nutritional counseling
  - If taking study drug, please bring any unused medications with you to this appointment for medication reconciliation (counting and inventory)
  - If you are in the control group, you will be weighed
- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit

This visit will take approximately 1 hour.

Visit 7 – Follow up visit (Week 8) Research Only
You will be asked to return to the BICRC research unit. If necessary, you may be scheduled for a home visit or a remote video visit and may receive your medication in person, by mail or curbside delivery. This visit will include:

- Treatment dispensing – based on your group assignment, you will receive either study medication or nutritional counseling; if in the control group, you will be weighed.
  - If taking study drug, please bring any unused medications with you to this appointment for medication reconciliation
  - If you are in the control group, you will be weighed
- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit

This visit will take approximately 30-45 minutes.

Visit 8 – Post-treatment visit (Week 10-11 [+/- 2 weeks]**) Research only****
You will be asked to return in a fasting state to the MARC research unit for:

- Vital signs
- Walk distance – to measure the distance you can walk over a period of 6 minutes
- Grip strength – using an instrument called a dynamometer that measures hand grip strength when you squeeze as hard as you can
- Isometric knee extension strength testing – to measure your leg strength, we will use a leg press machine like you would see in the gym
- DEXA scan – we will measure the total amount of fat and muscle in your body by a technique called Dual Energy X-ray Absorptiometry. During this procedure, which will last about 10 minutes, you will lie on an imaging table while an x-ray camera passes over your body from head to foot. The distance between the camera and your body will be about two feet. During the DEXA study, you will have to lie flat on your back. You will receive a small amount of radiation during the test. Other than this, there are no known risks associated with this exam.
- Liver fibroscan – we will perform a test that uses ultrasound to measure the amount of fibrosis (thickening or scarring of tissues) in your liver. It can be used alone or with other tests (such as biopsy, blood tests, ultrasounds) to see how much scarring there is on your liver. Fibroscanning is a pain-free diagnostic test that uses an ultrasound wand placed on your abdomen in the right upper quadrant where the liver is located using a lubricant gel to create a special image of your liver. The procedure usually takes about 5-10 minutes.
- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit

Your appointment for Visit 8 will take about 2 hours.

Visit 9 – Post-treatment visit (Week 10-11 [+/- 2 weeks]**) Research only****
You will be asked to go to the UT Health San Antonio Research Imaging Institute (RII) to undergo:

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- Magnetic Resonance spectroscopy (MRS) and Magnetic Resonance Imaging (MRI) of the liver to assess the intrahepatic liver fat (same as in Visit 3)

This visit will take approximately 1.5 hours.

** Visits 8 and 9 may be performed in reverse order based on scheduling availability of the DEXA and MRI scans.

Visit 10 – Post-treatment visit (Week 11-12) Research only {Optional}
You will be asked to present to the BICRC where you will undergo:

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- Cardiopulmonary (heart and lung) exercise testing (CPET/VO2max) – cycling on a stationary bike to determine how much oxygen your body requires during 10 minutes of endurance exercise. As part of this assessment, you will receive a 12-lead electrocardiogram (test which measures the electrical activity of your heart) (ECG) to monitor your heart rate and rhythm while you exercise while measuring the level of oxygen you require and carbon dioxide that is produced as a result.
  - This visit is optional. You may choose to not complete this visit by initialing below:

    _____ I do not wish to complete Visit 10 (heart and lung exercise testing and electrocardiogram)

This visit will take approximately 1 hour.

Visit 11 – Post-treatment visit (Week 11-12) Research only
You will be asked to present in a fasting state to the BICRC where you will undergo:

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- Muscle and fat biopsies like in Visit 5.
- You will also have blood and urine collections for research purposes (like Visit 5) as well as blood collection for safety labs like Visit 1 (CBC, CMP, Lipids, HbA1c, insulin, FFA).

This visit will take approximately 1 to 1.5 hours.

Visit 12 – Post-treatment visit and end of study (Week 13) Research only
You may be scheduled for a home visit, a telephone visit or a remote video visit. This visit will include:

- Assessment of adverse events – we will ask you if you have had any untoward medical experiences since the last visit
- We will check the sites of muscle and fat biopsy for healing wounds

This visit will take less than 30 minutes.

Title of Study: Effect of SGLT2 inhibition on aging-related biomarkers in older obese adults with pre-diabetes

Visit Schedule Summary

	VISIT 1	VISIT 2**	VISIT 3**	VISIT 4	VISIT 5	VISIT 6	VISIT 7	VISIT 8***	VISIT 9***	VISIT 10	VISIT 11	VISIT 12
Schedule	-17 days to -21	-7 days to -17, +/- 2wks	-7 days to -17, +/- 2wks	-1 days to -6	Day 0	Week 4	Week 8	Week 10-11, +/- 2wks	Week 10-11, +/- 2wks	Week 11-12	Week 11-12	Week 13
Consent	X											
Vital Signs	X	X						X				
Medical History	X											
Physical Exam	X											
MoCA	X											
Safety Labs (fasting):												
CBC	X										X	
CMP	X					X					X	
Lipid Panel	X										X	
PT/PTT/INR	X											
HbA1c	X										X	
Insulin	X										X	
FFA	X										X	
TSH	X											
Routine UA	X											
DXA		X						X				
Liver Fibroscan		X						X				
MRS/MRI - RII			X						X			
Physical Performance:												
Walk Distance		X						X				
Grip Strength		X						X				
Isom. Knee Ext		X						X				
VO2max CPET*				X						X		
Muscle Biospy					X						X	
SQ Fat Biopsy					X						X	
Research Labs:												
Blood					X						X	
Urine					X						X	
Nutrition consult and weight (controls)					X	X	X					
Nutrition Phone Follow Up					weekly	weekly	weekly					
Treatment dispensed					X	X	X					
Treatment Phone Follow Up					V5 +1w	V6+2w	V7+2w					
Biopsy check						X						X
Assess AE		X	X	X	X	X	X	X	X	X	X	X

*V02max CPET is optional (Visit 4 & 10)

**Visits 2 and 3 may be performed in reverse order

***Visits 8 and 9 may be performed in reverse order

Future Use of Your Information or Biospecimens Collected as Part of Your Participation

Identifiers may be removed and the de-identified information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

Your biospecimens, even if identifiers are removed, may be used for commercial profit and you would not share in this commercial profit.
Research involving your biospecimens might include whole genome sequencing and epigenetic analyses. Whole genome sequencing is the process of determining the complete DNA sequence of a person or other organism's genome at a single time. DNA is short for deoxyribonucleic acid. DNA contains information that determines, in part, the traits that are passed on from parent to child, such as eye color, height, or disease risk. Epigenetic analyses refer to changes that affect gene activity and expression.

Return of Research Test Results for Genetic Tests to Subjects

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk.

There are no plans to provide this information to you or your physician unless the information indicates that you may be at risk for a serious illness known at the time of testing to be treatable and it can be confirmed by a clinical laboratory. In that case, we will attempt to notify you using the contact information you have provided.

Ending Participation Early

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is stopped.

The researchers will discuss your options for medical care when your participation in this study ends.

Risks – "What are the risks of participation in the research?"

Risks from the specific research procedures (drug(s), interventions, or procedures)
The following section will describe the risks related to your participation in this research study. One risk is that you may have side effects while on the study. Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life-threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

Side effects from this study will usually go away soon after you stop taking the drug. In some cases, side effects can be long-lasting or may never go away.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to each drug, intervention or procedure that is part of this research study. You should talk to your study doctor about any side effects or other problems that you have while taking part in the study.

Risks and side effects related to the study include those which are:

Questionnaire data collection

Less likely (less than 5-30subjects out of 100) and Not Serious:

- Uncomfortable answering questions –If you feel uncomfortable answering questions, one of the investigators will speak with you to help clarify your doubts. Your responses will be kept confidential. You do not have to respond to any question that you do not feel comfortable answering.

Rare (less than 5 subject out of 100) and Serious:

Breach of confidentiality- It is possible in a rare occurrence there may be a breach of confidentiality. However, the researchers have taken steps to minimize this risk such as keeping focus group audio recordings and materials in a secure, locked location.

Physical assessment

Not Serious and Less Likely (less than 5-30 subjects out of 100) :

- Brief, temporary fatigue with walking 10-ft and/or using handheld dynamometer to measure grip strength
- There is minimal risk of injury during the lower extremity strength testing. You will be asked to slowly increase your exertion and to stop if any abnormal discomfort is felt.

Needlestick blood draw:

Likely, and may not be serious (5-30 subjects out of 100):

- Some people experience bleeding, bruising or swelling at the site of the needle entry. Fainting or lightheadedness may, also, occur. A qualified phlebotomist will perform your blood draw.

Less likely, and may or may not be serious (1-5 subjects in 100):

- Bleeding may occur outside of the blood vessels (hematoma).

Rare, and may or may not be serious (less than 1 in 100 needlestick procedures):

- There is a small risk of infection and nerve damage at the needle entry site.

Catheter blood draw:

Not serious and Less Likely (less than 1 in 100):

- During the study catheters may be inserted into the veins in your arm. Some people experience mild pain from the catheter.
- There is a small risk of bleeding when veins are punctured and a catheter is placed into the vein.
- Bleeding will be seen as bruising (black and blueness) at the place where the blood was obtained. The bruising usually goes away within 3 to 4 days, although sometimes it may take a week. The bruising is helped by using hot packs.
- There is a small risk of infection where your veins are punctured.

Muscle biopsy:

Less likely and not serious (1-2 in 100):

- At the time the muscle is obtained, most people feel a pressure sensation, and some people feel a thumping sensation.
- People might feel cramping, pain or soreness. In the people who feel cramping, pain or soreness, this will usually be mild to moderate in severity and will last 5 to10 seconds. The pain stops when the needle is removed, but your muscle may be sore for a few days.
- Bleeding from a muscle biopsy may occur will be seen as bruising at the place on your leg where we take the muscle. The swelling or bruising usually goes away with rest within 2-3 days, although sometimes it may take a week. The bruising is helped by using hot packs.

Rare and Serious (less than 1 in 500 of these procedures):

- Rarely, bleeding from a muscle biopsy may be severe enough to require hospitalization.

Rare and Serious (less than 1 in 1,000)

- Very rarely some subjects may experience numbness or tingling at the biopsy site. This usually is temporary and goes away in a few days. There is the possibility that nerve damage could be permanent.

Rare and Serious (less than 1 in 100)

- There is a small risk of infection at the site of the muscle biopsy. Symptoms of an infection would include pain, redness, swelling, and yellow-greenish (pus-looking) discharge in the biopsy site, and is usually accompanied by fever. Because multiple biopsies of the muscle will be performed, the risk of infection and pain in the leg may increase. Infections can be usually treated effectively with antibiotics taken by mouth. In very rare occasions, hospitalization is required to give antibiotics through the vein, and an operation could be needed to clean the infected area.
- Allergic reactions to the local anesthetic we use for the muscle biopsy are extremely rare, but could include a skin sore, swelling, or hives.

There is the possibility that a future biopsy may not be done at the discretion of the PI in case the subject did not tolerate well a prior biopsy.

Risks from Radiation Exposure

Risks from radiation exposure for the optional body composition:
Participation in this portion of the research study involves exposure to radiation from DXA scans. The amount of radiation exposure that you will receive from this procedure is equivalent to a uniform whole-body dose of 0.2 mrem (a unit of radiation exposure) which is less than 0.1 percent the average amount of radiation exposure (620 mrem dose) that each member of the general public receives per year. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (abnormal cells) or cancer. However, the probability of harm from such risk associated with the amount of radiation exposure that you will receive from this study is considered to be low when compared to other everyday risks each member of the general public receives per year, depending on the amount of radiation you personally have been exposed to in the past, particularly in the previous year.

The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other medical tests outside of this study that are a part of your medical care. Radiation risk builds up with each exposure. You should think about your own history of radiation exposure from tests (like x-rays or CT scans) in deciding about the radiation in this study. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

The following are the risks associated with treatment of **Dapagliflozin:**
Less likely and not serious:
These risks are expected to occur in 5-30 subjects or less out of 100 subjects:

- Diarrhea,
- Constipation,
- GI upset,
- Dizziness,
- Fatigue,
- Headache,
- Runny nose,

In Less than 4 out of 100 individuals

- Low blood sugar (also called Hypoglycemia),
- Urinary tract (about 1 out of 100 subjects) and genital infections (about 4 out of 100 subjects)

Rare and serious:

- Loss of consciousness (or syncope),
- Decrease in blood pressure (less than 1 out of 100 subjects),

Safety considerations for dapagliflozin and other SGLT2 inhibitors:
Dapagliflozin – is a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus and is a member of a class of antidiabetic medications that work by increasing the glucose excretion in the urine. Dapagliflozin (FARXIGA) has been approved by the U.S. FDA. Side effects reported with dapagliflozin will be summarized below based upon the package insert from the drug manufacturer Astra Zeneca.

(1) Hypotension

Dapagliflozin may cause intravascular volume contraction. Symptomatic hypotension can occur after initiating dapagliflozin particularly in patients with impaired renal function (eGFR less than 60 ±5 mL/min/1.73 m2), elderly patients, or patients on loop diuretics. Subjects with eGFR less than 60 ±5 ml/min/1.73 m2 will not be allowed in the study. Signs and symptoms of hypotension after initiating therapy will be monitored. If a participant experiences any of these, the dapagliflozin will be stopped and the participant will be discontinued from the study.

(2) Renal Function

A small decrease in kidney function (eGFR) and increase in serum creatinine has been observed when dapagliflozin is initially started. The eGFR gradually returns toward normal while the drug is continued and returns to normal if drug is stopped. If the eGFR drops below 60 or if the serum creatinine rises by ≥3 mg/dl the dapagliflozin will be stopped and the participant will be discontinued from the study.

Sudden kidney injury (acute kidney injury) has happened to people taking dapagliflozin. Talk to your doctor right away if you:

- reduce the amount of food or liquid you drink for example, if you are sick or cannot eat or
- you start to lose liquids from your body for example, from vomiting, diarrhea or being in the sun too long. Seek medical attention immediately if you experience signs and symptoms while taking these medicines such as:
    - Decreased urine
    - Swelling in your legs or feet

(3) Hypoglycemia

Hypoglycemia (low blood sugar) – can occur with any antidiabetic medication. In studies of dapagliflozin, the frequency of hypoglycemia was less than 5% and similar to that in the placebo group. Subjects will be told to call the investigator if symptoms (sweating, rapid thumping heartbeat, mental confusion) of hypoglycemia occur and to drink a glass of orange juice with a packet of sugar. Any subjects with hypoglycemia will be evaluated for potential causes. If the hypoglycemia recurs, the subject will be discontinued from the study.

(4) Serious urinary tract infections

Serious urinary tract infections that may lead to hospitalization have happened in people who are taking dapagliflozin. Tell your doctor if you have any signs or symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often, the need to urinate right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting. You should seek medical attention and contact your study doctor immediately if you experience any of these symptoms.

(5) Genital Mycotic Infections

Vulvovaginitis, balanitis and related genital infections were reported in 4.8% and 0.9% of subjects who received dapagliflozin 10 mg and placebo, respectively. Most infections were mild to moderate, and subjects responded to an initial course of standard treatment and rarely resulted in discontinuation from dapagliflozin treatment. These infections were more frequent in females (6.9% and 1.5% for dapagliflozin and placebo, respectively), and subjects with a prior history were more likely to have a recurrent infection.
If you experience a genital infection call the study doctor. You will be treated with a local antifungal cream or oral antibiotic therapy.

(6) Necrotizing Fasciitis of the perineum (or Fournier's gangrene)

Cases of a rare, but serious, infection of the genitals and areas around them have been reported with the drug class, SGLT2 inhibitors, like dapagliflozin. This serious condition, called necrotizing fasciitis of the perineum or Fournier's gangrene, is a life-threatening infection requiring urgent antibiotics and surgical intervention.

Seek medical attention immediately if you experience any symptoms of tenderness, redness, or swelling of the genitals or the area from the genitals back to the rectum, and have a fever above 100.4°F or a general feeling of being unwell. These symptoms can worsen quickly, so it is important to seek treatment right away. Serious outcomes have included hospitalization, multiple surgeries, and death.

(7) Volume depletion

Dapagliflozin increases the amount of salt and water that is excreted in the urine. Reactions related to volume depletion (including dehydration, hypovolemia, orthostatic hypotension, or hypotension) were reported in 0.8% and 0.4% of subjects who received dapagliflozin 10 mg and placebo, respectively; serious reactions occurred in < 0.2% of subjects balanced between dapagliflozin 10 mg and placebo.
Call the investigator if you experience symptoms of volume depletion.

(8) Malignancies

During clinical trials, the overall proportion of subjects with malignant or unspecified tumors was similar between those treated with dapagliflozin (1.47%) and placebo/comparator (1.35%), and there was no carcinogenicity or mutagenicity signal in animal data. When considering the cases of tumors occurring in the different organ systems, the relative risk associated with dapagliflozin was above 1 for some tumors (bladder, prostate, breast) and below 1 for others (e.g. blood and lymphatic, ovary, renal tract), not resulting in an overall increased tumor risk associated with dapagliflozin. The increased/decreased risk was not statistically significant in any of the organ systems. If you have a prior history of bladder, prostate, or breast cancer please tell us.

(9) Bone Health

Bone mineral density measurements in patients with normal or mildly impaired renal function did not indicate bone loss over a treatment period of one year, and there was no increase in fracture risk in these individuals with normal or mildly impaired renal function. However, it cannot be excluded that with longer periods of treatment there will be a decrease in bone mineral density or increase in bone fracture risk.
If you experience a bone fracture contact the study doctor.

(10) LDL Cholesterol

A small increase in LDL cholesterol of about 4% has been observed in diabetic patients treated with dapagliflozin.

(11) Cardiovascular Events

No increased risk of cardiovascular events (myocardial infarction, stroke, cardiovascular death) has been observed with dapagliflozin. Any participant who experiences a stroke or myocardial infraction will be discontinued from the study and the IRB and sponsor will be notified. If these individuals should experience a cardiovascular event while taking dapagliflozin, we discontinue them from the study.

(12) Hypersensitivity Reactions

Severe hypersensitivity reactions, including angioedema and urtricaria have been reported in patient taking dapagliflozin, although a causal association has not been established. Serious anaphylactic reactions and severe cutaneous adverse reactions and angioedema were reported in 0.2% of comparator-treated patients and 0.3% of dapagliflozin-treated patients. If such a reaction occurs in any participants, the dapagliflozin will be stopped and the subject will be discontinued from the study.

(13) Pre-clinical Concerns

Dapagliflozin did not induce tumors in either mice or rats at any of the doses evaluated in 2-year carcinogenicity studies. There was no carcinogenicity or mutagenicity signal in animal studies, suggesting that dapagliflozin does not represent a genotoxic risk to humans.

The U.S Food and Drug Administration has warned that the use of dapagliflozin (a class of drugs, called sodium-glucose cotransporter-2 (SGLT2) inhibitors) may lead to ketoacidosis, a serious condition where the body produces high levels of blood acids called ketones that may require hospitalization. You should pay close attention for any signs of ketoacidosis and seek medical attention immediately if you experience symptoms such as difficulty breathing, nausea, vomiting, abdominal pain, confusion, and unusual fatigue or sleepiness. Do not stop or change your diabetes medicines without first talking to your prescriber. Your doctor will evaluate for the presence of acidosis, including ketoacidosis, if you are experiencing these signs or symptoms; discontinue SGLT2 inhibitors if acidosis is confirmed; and take appropriate measures to correct the acidosis and monitor sugar levels.

If the study doctor is not available and your symptoms do not improve seek immediate emergency medical care if necessary.

Do not stop or change your diabetes medicines without first talking to your prescriber. Your doctor will evaluate for the presence of acidosis, including ketoacidosis, if you are experiencing these signs or symptoms; discontinue SGLT2 inhibitors if acidosis is confirmed; and take appropriate measures to correct the acidosis and monitor sugar levels.

If any participant develops any sort of tumors, the Dapagliflozin will be discontinued and the IRB and sponsor will be notified.

Risks and Side Effects Related to Electrocardiogram (ECG):

Rare and not Serious:

In 100 people, approximately 5 or less may have:

- Mild skin irritation (e.g., itching, rash), occurring where the electrodes are stuck on the skin
- Discomfort from lying in one position for 5 – 10 minutes while the ECG is being recorded

Risks related to MRI Scanning

Less Likely, and Not Serious

In 100 people, approximately 10 or less may have:

- Skin or eye irritation caused by the dyes from tattoos or tattooed eyeliner

- Slight warming of the body due to prolonged exposure to radio waves during the MRI
- Claustrophobia or psychological distress during the scan. All equipment and testing will be explained to you prior to the beginning of testing. Usually, conversation and reassurance will remove any anxieties. If you experience severe anxiety during the study, you are free to end the session.

Less likely and serious
In 100 people, approximately 5 or less may have:
Implanted metal devices or artificial limbs may malfunction or cause injury

For more information about risks and side effects, ask one of the researchers or study staff.
We will tell you about any significant new findings which develop during the course of this research which may relate to your willingness to continue taking part.

Risks related to home visits:
During home visits there is a risk of improper disclosure or loss of research records and research specimens. When necessary to perform home visits, the study staff will use precautions to reduce these risks. The study staff will not remove any of your original records from the research clinical site and will only use the minimal amount of protected health information necessary to accomplish the home visit. The study staff will keep study records in a locked file case. Research specimens will be labeled and packed according to the study site's laboratory requirements and returned to the research site (FORU) in a carrier designated for biohazardous materials. Study records and specimens will never be left unattended during the home visit or when being transported to and from the study site.

Risks related to remote and/or virtual visits:
Due to the use of online conferencing systems, your privacy and confidentiality is not guaranteed. The research staff will use precaution during these visits and will not collect any information that could be damaging to your financial standing, employability, insurability and reputation.

Fitbit Bluetooth Scale: You will be provided with a Fitbit Bluetooth Scale and the associated email/password to login into the Fitbit user account. Research staff will be able to access, view, and download fitbit data through the Fitbit platform. Agreeing to participate in this study is an acceptance of the Fitbit Terms of Use and Privacy Policy.

Genetic Informational risks related to the study
This study will/may include genetic testing. Human tissue contains genes that determine many of a person's physical characteristics, such as the color of eyes and hair. In some cases, genetic testing of tissues can be used to indicate a risk for the development of certain diseases. Genetic information is unique to each individual and could potentially be used to discover possible changes in a person's future health status or life expectancy, or that of his/her children and family members. Even if your tissues are used for this type of research, the results will not be put in your health records. Releasing this information to you could cause psychological distress, anxiety or family problems.

Releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increase difficulty in obtaining or maintaining disability, long-term care, or life insurance.

These risks would occur if your information is released by mistake. The measures being taken to protect your privacy are discussed below and make this possibility unlikely.

Even though the results of genetic testing may not be linked to you, it is possible that people of your ethnic background may be found to be at more risk for certain diseases based on future genetic research and this

information might harm you in the future as a member of the group. Also, there may be unknown risks of genetic testing in the future.

Are there Risks related to withdrawing from the study?
If you decide to withdraw from this study early, please discuss your decision with the principal investigator. The researcher will ask you to complete study withdrawal procedures at a final study visit. This visit would include as much as possible of the post-treatment data collection (visits 8-11). There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

Reproductive Risks
Women who are not post-menopausal, and less than 60 years of age, cannot take part in this study.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time, may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section "Contact Information" for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – "How could you or others benefit from your taking part in this study?"
The possible benefit of your participating in this study is to receive updated lab results related to your blood sugar. You will also receive compensation for participation which could be of small benefit to you.

We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"
There are other options available to you. Your other choices may include:

Treatment of elevated blood sugar (pre-diabetes or impaired glucose tolerance) using other treatments such as nutritional counseling, diet and exercise, or the medication metformin. You may also choose not to get any other treatment.

Payments – Will there be any payments for participation?
The researchers will provide you with a MasterCard®. Compensation will be automatically credited after completion of each study visit that includes a reimbursement to you for your time and the cost of parking. If you complete all visits and procedures, the total compensation will be $540.00. Your name, address and date of

birth will be shared with a third-party solely for the purposes of compensation processing. This information will only be used for the administration of the compensation (ClinCard) and will be kept strictly confidential.

Visit 1	$25
Visit 2	$40
Visit 3	$40
Visit 4-optional	$25
Visit 5	$125
Visit 6	$15
Visit 7	$25
Visit 8	$40
Visit 9	$40
Visit 10-optional	$25
Visit 11	$125
Visit 12	$15
Manual Payment (unscheduled visit, lab visit, or AE)	Up to $50

In addition to the compensation on the card, you may also elect to receive study-related messages (text and/or email). These messages may contain information confirming that money has been loaded onto your card. You may also receive reminder messages with information about your next appointment with researchers or study staff.

Please indicate your willingness to receive study-related messages:

- □ **Yes,** I would like to participate (please select the best method(s) for communication)
  - Cell Phone (text messages)
  - Email
- □ **No,** I choose not to participate

If you are paid, the money you receive may be taxable. When the total of any study payments is $600 or more in one calendar year, the institution must report the amount to the IRS. The IRS considers it earned income and treats it like any other income.

Costs – Will taking part in this study cost anything?

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study, such as an illness, medication, or adverse event that is not study related. It is important to understand that some insurance companies do not cover some costs (for example, approved drugs used in a way different from the package instructions). If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the researchers if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

The Principal Investigator will provide the study drug free of charge during this study. At the end of your participation you must return all unused study drug to the researcher.

There will be no direct cost to participating in the study. The Fitbit Bluetooth Scale can be used at no additional cost. However, there may be additional charges to your cellular phone plan due to use of text messages and the telehealth portal depending on your cellular data plan.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the Federal Government. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under certain circumstances. Circumstances that warrant the release of your information without your permission include: abuse and/or neglect, intention to harm yourself or others, or certain communicable diseases.

Limits of Confidentiality
Even without your consent, suspected or known abuse or neglect of a child, disabled, or elder abuse, threatened violence to self or others or other local health reporting requirements will be reported to appropriate authorities.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study.

What is Protected Health Information (PHI)?
Protected Health Information is information about a person's health that includes information that would make it possible to figure out whose it is. According to the law, you have the right to decide who can see your protected health information. If you choose to take part in this study, you will be giving your permission to the investigators and the research study staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include: medical history, blood work, information gathered from your medical record if available, treatments prior to the study, information you provide during participation in the study, results of blood tests, and demographic information like your age, marital status, race or ethnicity, and education you have completed.
We will get this information by asking you, asking your doctor, and by looking at your chart if one is available at UT Health San Antonio or University Health System (including Texas Diabetes Institute).

How will your PHI be shared?
Because this is a research study, we will be unable keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

- the UT Health San Antonio Claude D. Pepper Older Americans Center the study
- the company (for example, McKesson) that provides the study drug
- the UT Health San Antonio Claude D. Pepper Older Americans Center Data and Safety Monitoring Board, which is the committee that checks the study data and safety on an ongoing basis, to determine if the study should be stopped for any reason.
- the members of the local research team
  the Institutional Review Board and the Compliance Office of the University of Texas Health Science Center at San Antonio, and other groups that oversee how research studies are carried out.

- the Research offices at UT Health San Antonio
- the Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug research

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of UT Health San Antonio MARC, or RII for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the researchers and other groups to see and share your health information. If you choose not to let the researchers and other groups use your health information, there will be no penalties, but you will not be allowed to participate in the study. After you enroll in this study, you may ask the researchers to stop using your health information at any time. However, you need to say this in writing and send your letter to **Dr. Carolina Solis-Herrera, Assistant Professor, Medicine-Diabetes, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.** If you tell the researchers to stop using your health information, your participation in the study will end and the study staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the study staff if you have a need to review your PHI collected for this study.
You will only have access to your PHI until 12/31/2029. Because of the type of research, you can only access your PHI when the study is done. At that time, you have the right to see and copy the medical information we collect about you during the study, for as long as that information is kept by the study staff and other groups involved.

How long will your PHI be used?
By signing this form, you agree to let us use and disclose your health information for purposes of the study until December 31, 2029. This permission to use your personal health information expires on the date noted above.

Contact Information – Who can you contact if you have questions, concerns, comments or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments or complaints later or you wish to report a problem which may be related to this study please contact:

Carolina Solis-Herrera, MD can be reached at (210) 567-6691 during normal business hours or after hours (for urgent medical issues) by calling 210-220-0445. In case of a medical emergency, please call 911 for assistance.

Primary contact:

- Carolina Solis-Herrera, MD can be reached at (210) 567-6691 during normal business hours.
- Nicolas Musi, MD, can be reached at (210) 617-5197 during normal work hours and (210) 630-5001 after business hours.

The University of Texas Health Science Center committee that reviews research on human subjects (Institutional Review Board) will answer any questions about your rights as a research subject, and take any concerns, comments or complaints you may wish to offer. You can contact the IRB by calling 210-567-8250, or by mail to IRB, UTHSCSA, Mail Code 7830, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.

Title of Study: Effect of SGLT2 inhibition on aging-related biomarkers in older obese adults with pre-diabetes

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information in this research sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE

- You have read the above information.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.

Adult Signature Section

- You have voluntarily decided to take part in this research study.
- You authorize the collection, use and sharing of your protected health information as described in this form.

Printed Name of Subject	Signature of Subject	Date	Time AM PM
Printed Name of Witness	Signature of Witness	Date	Time AM PM

☐ *Check if consent and authorization obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. Have witness initial below.*

Declaration of witness: I was present for the entire consent process. _____ ←(initials of witness)

Printed Name of Person Obtaining Consent and Authorization	Signature of Person Obtaining Consent and Authorization	Date	Time AM PM

☐ Consent and authorization was obtained from this individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. The method used for communication with the subject was: _____.

The specific means by which the subject communicated agreement to participate was:

_____

Please indicate whether you give your permission to be videotaped during remote and/or virtual visits:

☐ Yes

Initials of participant or individual authorized to consent on behalf of the participant	Date

☐ No

Initials of participant or individual authorized to consent on behalf of the participant	Date