COVER PAGE

Official Study Title: The Effect of GLP1 Receptor Agonists on Physical Function, Body Composition, and Biomarkers of Aging in Older Overweight/Obese Adults with Insulin Resistance

NCT number: NCT05786521

IRB Approval Date: 08.30.2023

Unique Protocol ID: 20220256HU

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. Insulin resistance (prediabetes or diabetes) is associated with sarcopenia (decrease muscle mass), functional decline, and an increase in known markers of biological aging. These factors are not usually considered in choosing medications for the treatment of diabetes. The purpose of this research is to evaluate whether older adults with prediabetes or diabetes can benefit from taking a diabetes drug called semaglutide (brand name Ozempic) in addition to lifestyle counseling to improve physical function, body composition, and biological markers of aging compared to lifestyle counseling alone.

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 medical history, physical examination, and screening blood tests. They will receive random assignments to either receive study medication and education on lifestyle modification or education on lifestyle modification alone over the course of about 6 months. Participants will complete pre- and post-treatment testing including evaluations of physical function by measures like grip strength, walking speed and distance, evaluation of body composition by a body composition scan (called a DXA scan), measurement of body mass index (BMI), surveys, and adipose (fat) and muscle samplings.

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?
The study involves a total of 8 visits over the course of approximately 20 weeks. Visits will occur at the start of the study, 3 weeks into the study, 7 weeks into the study, 11 weeks into the study and at the end of the study. During the study, you may have televisits (phone or virtual visits) for lifestyle modification education or checking on your progress. The longest in-person visits will be the second and the sixth visit due to assessments and procedures needing completion, approximately 4 hours. The other in-person visits should each last approximately 2 hours.

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, but you may benefit from learning more about lifestyle changes and receiving study-related clinical care that is at no cost to you. There is a small amount of reimbursement for your time and travel to the research unit.

The risks associated with your participation may include side effects of the study medication, pain or bleeding from the blood draws or adipose and muscle biopsies, emotional distress from assessments, or fatigue from physical performance measures. The DXA scan does have a small amount of radiation.

For more information, please *see* ***How could you or others benefit from your taking part in this*** and ***What are the risks of participation in the research*** sections below.

5. What else should I consider before I make my decision?
This study will involve attending study visits at the Barshop Institute Clinical Research Unit (BICRU) 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.

Consent to be part of a Research Study
To be conducted at
University of Texas Health Science Center at San Antonio (UT Health 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 Tiffany Cortes, MD, Assistant Professor, UTHSA Department of Medicine, Endocrinology Division.

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 is to evaluate whether older adults with prediabetes or diabetes can benefit from taking a drug called semaglutide (Brand name Ozempic) in addition to lifestyle counseling to improve physical function, body composition, and biological markers of aging compared to lifestyle counseling alone.

You are asked to participate in this research study of prediabetes/diabetes and aging. This study specifically addresses decreased physical function and lean mass that occurs with insulin resistance aging. The researchers hope to learn whether semaglutide in addition to lifestyle counseling can help improve physical function, body composition, and biomarkers of aging for treatment of older patients with prediabetes or diabetes. This could help influence the types of medications used in the treatment of older adults with insulin resistance.

Investigation Use of Drug or Device
This study involves the use of an investigational drug called semaglutide (brand name Ozempic). "Investigational" means that the drug has not yet been approved by the U.S. Food & Drug Administration (FDA) for pre-diabetes treatment or for improvement of physical function and biomarkers of aging. This medication is approved for use in diabetes and weight management.

This study will compare the effects, good and/or bad, this drug has on people who take it and its effect on physical function and muscle mass in older adults with pre-diabetes or diabetes. The safety of this drug in humans has been tested in prior research studies; however, some side effects may not yet be known.

This trial may be registered on www.ClinicalTrials.gov, a publicly available registry of clinical trials. 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 65 years of age or older, with a BMI greater than or equal to 27 kg/m^2 and have prediabetes or diabetes.

How many people are expected to take part in this study? This study will enroll approximately 20 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 8 visits with the researchers or study staff over approximately 6 months. You will spend between 1 and 4 hours at each visit, depending on the procedures being done. It may be necessary for you to return to clinic every 2-4 weeks during the study. All in-person visits will occur at Barshop Institute for Longevity and Aging Studies.

Study Procedures- as a participant, you will undergo the following procedures:

Visit 1, Screening and Baseline Testing, Research only

This visit will take approximately 2 hours and will occur at the Barshop Institute. You will be asked to arrive fasting to the research unit for this visit. After the consent is signed, you will undergo screening and baseline testing procedures as outlined below. 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.

Outline of visit

- Informed Consent- We will review all details of the research program in private. You will be provided with adequate time to have your questions answered, concerns addressed or clarified, and for you to consider whether or not you wish to participate. You will be given a copy of the informed consent to keep.
- Medical history & physical exam/assessment
  - Routine vital signs like blood pressure, heart rate, height, weight, etc will be obtained.
  - Detailed medical history including illnesses, surgeries, social habits, medications and allergies will be obtained.
  - Physical exam similar to one at your primary physician's office will performed.
- Electrocardiography (ECG)- a test used to evaluate your heart's electrical function. Stickers are put on your skin on your chest, arms and legs; these stickers have electrodes that are connected to the machine by lead wires.
- Screening labs- a blood draw, approximately 2 tablespoons, will be drawn and used to assess your general health status. The following blood tests will be performed:
  - Complete blood count (CBC) with differential
  - Comprehensive metabolic panel (CMP)
  - Lipid panel
  - Hemoglobin A1c (HbA1c, a 3-month average reading of blood glucose levels)
  - Thyroid stimulating hormone (TSH, an indicator of your thyroid function)
  - Coagulation test (PT/PTT/INR) to assess how fast your blood will clot
- Physical function testing, which will include:
  - Balance when standing
  - Distance able to walk over a period of 6 minutes

- Time it takes to walk about 10 feet
- Time it takes for you to quickly stand up from a chair and sit down on a chair multiple times
- Grip strength using an instrument called a dynamometer that measures strength when you squeeze as hard as you can

❖ DXA 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 DXA study, you will have to lie flat on your back. You will receive a small amount of radiation during the test.

❖ Completing a quality of life and appetite survey.

This appointment for Visit 1 will take about 2 hours.

Visit 2 (Day 0), Research only

Eligible participants asked to arrive fasting to the Barshop Institute research unit to undergo the following:

❖ Vital signs – typical assessments like blood pressure, heart rate, respiration rate, and temperature

❖ Blood draw – Similar to blood draw at Visit 1. Approximately 2 tablespoons will be drawn for research-only to analyze blood markers that are thought to be related to aging.

❖ Muscle biopsy
- We will take 1-2 small 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 pressure. The pain is mild to moderate and lasts 30 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. If you know you are allergic to adhesives used in these types of devices, we can suture your skin and have you return to remove the stitches.

❖ 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 a 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.
- After the sample is obtained, we will apply a bandage and cover it for protection. We will instruct you how to care for the wound.

❖ **Assignment to Study Groups**:
- You will be randomized, assigned by chance (flipping a coin), to one of two study groups.

- Study group 1 will take the study drug (open label), semaglutide (Ozempic), starting at 0.25 mg subcutaneous injection with titration up to 1 mg per week plus standard lifestyle counseling, -or-
- Study group 2 will receive standard lifestyle counseling without a study drug.

- Everyone will have lifestyle counseling. This will be focused on education about healthy eating and physical activity. Throughout the study, these visits may be conducted in person, by video or phone.
- Specifically for study group 1 (study medication plus lifestyle counseling):
  - You will be supplied the medication at this visit and taught how to self-administer the subcutaneous injection of semaglutide 0.25 mg.
  - You will be monitored on your first self-injection.
  - You will be started on the medication.

Your appointment for Visit 2 will take about 2-3 hours.

Visit 3 (Approximately week 3), Research only

- Vital signs – Typical assessments like blood pressure, heart rate, respiration rate, temperature, weight
- Assessment of adverse events- We will ask you if you have had any (unexpected) medical experiences (events) since the last visit.
- Continuation of lifestyle counseling
- Specifically for study group 1 (study medication plus lifestyle counseling)
  - Study medication will be distributed.
  - We will review how well you have been able to take the medication and review administration self-injection instructions.
  - Depending on how you tolerate the medication, we will instruct you how to increase the dose of semaglutide to 0.5 mg.

Your appointment for Visit 3 will take about an hour.

Visit 4 (Approximately week 7), Research only

- Vital signs – typical assessments like height, weight, blood pressure, heart rate, respiration rate, and temperature
- Assessment of adverse events- we will ask you if you have had any (unexpected) medical experiences (events) since the last visit.
- Continuation of lifestyle counseling
- Specifically for study group 1 (study medication plus lifestyle counseling)
  - Study medication will be distributed.
  - We will review how well you have been able to take the medication and review administration self-injection instructions.
  - Depending on how you tolerate the medication, we will instruct you how to increase the dose of semaglutide to 1 mg.

Your appointment for Visit 4 will take about an hour.

Visit 5 (Approximately week 11), Research only

- Vital signs – typical assessments like height, weight, blood pressure, heart rate, respiration rate, and temperature
- Assessment of adverse events- we will ask you if you have had any (unexpected) medical experiences (events) since the last visit.
- Continuation of lifestyle counseling
- Specifically for study group 1 (study medication plus lifestyle counseling)

- Study medication will be distributed.
- We will review how well you have been able to take the medication and review administration self-injection instructions.
- Depending on how you tolerate the medication, we will either continue or decrease the semaglutide dose.

Your appointment for Visit 5 will take about an hour.

Visit 6a (Approximately week 20), Research only

Participants asked to arrive fasting to the Barshop Institute research unit to undergo the following:

- Physical exam/assessment
  - Routine vital signs like blood pressure, heart rate, height, weight, etc will be obtained.
  - Physical exam similar to one at your primary physician's office will performed.
- Assessment of adverse events- we will ask you if you have had any (unexpected) medical experiences (events) since the last visit.
- Blood draw - Similar to blood draw at Visit 1. Approximately 2 tablespoons will be drawn to assess your general health status. The following lab tests will be performed:
  - Complete blood count (CBC) with differential
  - Comprehensive metabolic panel (CMP)
  - Lipid panel
  - Hemoglobin A1c (HbA1c, a 3-month average reading of blood glucose levels)
  - Thyroid stimulating hormone (TSH, an indicator of your thyroid function)
  - Coagulation test (PT/PTT/INR) to assess how fast your blood will clot
- Physical function testing which will include:
  - Balance when standing
  - Distance able to walk over a period of 6 minutes
  - Time it takes to walk about 10 feet
  - Time it takes for you to quickly stand up from a chair and sit down on a chair multiple times
  - Grip strength using an instrument called a dynamometer that measures strength when you squeeze as hard as you can
- DXA 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 DXA study, you will have to lie flat on your back. You will receive a small amount of radiation during the test.
- Completing a quality of life and appetite survey.

Your appointment for Visit 6a will take about two hours.

Visit 6b (Approximately week 20), Research only

Participants asked to arrive fasting to the Barshop Institute research unit to undergo the following:

- Vital signs – typical assessments like blood pressure, heart rate, respiration rate, and temperature
- Assessment of adverse events- we will ask you if you have had any (unexpected) medical experiences (events) since the last visit.
- Blood draw – Similar to blood draw at Visit 2. Approximately 2 tablespoons will be drawn for research-only to analyze blood markers that are thought to be related to aging.
- Muscle biopsy
  - We will take 1-2 small 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 pressure. The pain is mild to moderate and lasts 30 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. If you know you are allergic to adhesives used in these types of devices, we can suture your skin and have you return to remove the stitches.

❖ 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 a 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.
- After sample is obtained, we will apply a bandage and cover it for protection. We will instruct you how to care for the wound.

Visit 7 (Approximately week 21), Research only

❖ The last visit can be in person or a televisit (phone or virtual) to ensure that you are doing well after visit 6a and visit 6b.

Visit Schedule Summary

	T - (1 wk ±7d)	T =0	T (3w ± 7d)	T (7w ± 7d)	T (11w ± 7d)	T (20w ± 7d)	T (20w ± 7d)	T (21w ± 7d)
Visit #	V1	V2	V3	V4	V5	V6a	V6b	V7
History and physical exam	X					X		
Vitals, anthropometric measurements	X	X	X	X	X	X	X	
Clinical labs	X					X		
Randomization		X						
DXA scan	X					X		
ECG	X							
SPPB, grip strength, 6-minute walk	X					X		
Surveys (SF-12, CNAQ)	X					X		
Blood, muscle, and adipose biopsy		X					X	
Semaglutide dispensed to treatment group		X	X	X	X			
In-person lifestyle education		X	X	X	X			
Assessment for adverse events			X	X	X	X	X	X

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. 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, such as eye color, height, or disease risk, that are passed on from parent to child.

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 and discuss recommended follow up.

Information about Optional Procedures – "What are other research activities that may be done but are not required for your participation?"

E-mail Authorization Agreement

The research team would like to communicate with you regarding your research visits via email, which uses an "encrypted" method for secure transmission. When one of the research team sends you an email, you will receive an email that says "[SECURE MESSAGE]" from a research team member with a link to open the message. When you click on the link it will take you to a secure website where you can read the message and reply after successful authentication.
If you are not able to receive email, you may not be eligible to participate in the study.

Texting

The research team would like to communicate with you regarding your participation via text message. These messages may include information related to your participation in the study and payment information, if applicable. In order to do this, we will share your name and phone number with Tiger Connect. Standard text messaging rates will apply if you do choose to receive the text messages.

If you are not able to receive texts, you may not be eligible to participate in the study.

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 study 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 may not 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 5-30 subjects 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, researchers have taken steps to minimize this risk such as keeping records and materials in a secure, locked location.

Physical function testing exam/assessment
Not Serious and Less Likely (less than 5-30 subjects out of 100):
- Brief, temporary fatigue with balance test, walking 10-ft and/or using handheld dynamometer to measure grip strength

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 to reduce the risk of this happening.

Less likely, and may or may not be serious (1-5 subjects in 100):
- Bleeding may occur outside of the blood vessels (hematoma/bruise).

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 to facilitate blood draw and reduce number of needlesticks. 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 subjects 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 approximately 30 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 and 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 reduced 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 may 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.

Adipose biopsy:
Likely and not serious:
- Numbness in the area
- Scar of ~5mm for each incision
- Bleeding from an adipose biopsy may occur and will be seen as bruising at the place on your abdomen where we take the adipose sample. The swelling or bruising usually goes away with rest within 2-3 days, although sometimes it may take a week.

Less likely and not serious:
- Moderate pain at the site where the sample was collected
- Skin irritation at the site of the bandage

- Reaction to the medication (Lidocaine) used to numb the area

Less Likely and serious (less than 1 in 100):
- Infection at the site where the sample was collected.

Radiation exposure for body composition (DXA)
Participation in this research study involves exposure to radiation from medical imaging (ex: Fluoroscopy, CT, PET, Nuclear Medicine scan). Every member of the general public receives approximately 310 mrem (a unit of radiation exposure) every year from natural sources, including cosmic radiation and radiation naturally found in our environment. Current evidence and research suggest that the risks of medical imaging at radiation doses below 10,000 mrem are too low to be detectable and may be nonexistent (American Association of Physicists in Medicine Policy PP 25, Health Physics Society Position Statement PS010-4). The total amount of radiation exposure that you are anticipated to receive from the procedures associated with your participation in this research study is 0.2 mrem, which is less than the amount of radiation exposure a member of the general public receives from natural sources per year on average.

If you have had prior radiation therapy (such as for cancer), or have any questions regarding radiation and its risks, please reach out to the Radiation Safety Office who can put you in touch with someone who can help address your concerns.

Semaglutide
The following are the risks possibly associated with treatment of Semaglutide (Brand name Ozempic):

Less likely and not serious (5-20 subjects out of 100):
- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Constipation
- Indigestion
- Gastritis (Inflammation of the lining of the stomach)
- Decreased appetite
- Increased flatulence (passing gas)
- Fatigue
- Headache
- Change in taste

Less likely and serious (1-4 subjects out of 100):
- Low blood sugar (also called Hypoglycemia)
- Gallbladder disease
- Worsening of diabetic retinopathy (eye condition that can cause vision loss and blindness)
- Injection site reactions
- Low blood pressure
- Dizziness
- Developing antibodies to Semaglutide

Rare and serious:
- Acute kidney injury
- Hypersensitivity reactions such as anaphylaxis and angioedema (allergic reactions)
- Acute pancreatitis including hemorrhagic pancreatitis and necrotizing pancreatitis

- Medullary thyroid carcinoma was seen in animal trials with other medications, not Semaglutide, in the glucagon-like peptide (GLP-1) receptor agonist class and medullary thyroid cancer has been reported in patients taking liraglutide (a similar medication).

Acute events of gallbladder disease such as cholelithiasis (gallstone formation) or cholecystitis (inflammation of the gallbladder) have been reported in GLP-1 receptor agonist trials and postmarketing. In placebo-controlled trials, cholelithiasis was reported in 1.5% and 0.4% of patients-treated with Ozempic 0.5 mg and 1 mg, respectively. Cholelithiasis was not reported in placebo-treated patients.

Electrocardiogram (ECG):
Rare and not Serious (5 or fewer subjects out of 100):

- 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

Genetic Informational risks related to the study
This study 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.

Changes to medications
Please immediately inform the study team when a new medication or supplement is started, as this may increase the risk of having an adverse event.

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 may ask you to complete study withdrawal procedures at a final study visit. This visit includes the procedures in visit 6a, 6b, and 7. There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

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?"

There is no guarantee or promise that you will receive any benefit from this study. However, the possible benefit of your participating in this study is to receive health information such as lab results related to your blood sugar, information on your body composition, and education on lifestyle modifications.

We hope the information learned from this study will benefit other people with similar conditions in the future. Physical function decline and loss of muscle mass are commonly seen in older adults, especially those with insulin resistance. Your participation may benefit future patients by helping us gain valuable information for conditions that affect a majority of older adults.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

Your other option would be to not participate in this study.

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 visit. Your name, address, date of birth, and social security number 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. The payment schedule is as follow:

Visit 1	$50
Visit 2	$125
Visit 3	$20
Visit 4	$20
Visit 5	$20
Visit 6a	$50
Visit 6b	$125
Visit 7	$15

The total you may receive if you completed all visits for this study is up to $425.

Costs – Will taking part in this study cost anything?

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

There is no direct cost to participating in the study.

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, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings or any other person not connected to the research, your (or your family member's) name or any of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, 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, or other scientific research that is in compliance with applicable Federal regulations governing the protection of human participants in research. Should you require medical treatment as it relates to the information, document, or biospecimen pertains, additional consent will be obtained.

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, and race or ethnicity.

We will get this information by asking you, asking your doctor, and/or looking at your electronic medical record if one is available through the UT Health San Antonio system.

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 National Institutes of Health (NIH), National Institute of Aging (NIA) who is funding the study
- The UT Health San Antonio Claude D. Pepper Older Americans Center, where the study is being conducted
- The company that provides the study drug (Medplus)
- 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.

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 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:

Tiffany M. Cortes, MD
4939 Charles Katz Dr.
San Antonio, TX 78229

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 12/31/2032.
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 the end of the study. This permission to use your personal health information expires when the research ends, and all required study monitoring is over.

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:

Primary contact:
Tiffany M. Cortes, MD can be reached at 361-244-3747

If primary is not available:
Sara E. Espinoza, MD can be reached at 210-617-5197

The UT Health San Antonio 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, UT Health San Antonio, Mail Code 7830, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900.

Title of Study: The Effect of GLP1 Receptor Agonists on Physical Function, Body Composition, and Biomarkers of Aging in Older Overweight/Obese Adults with Insulin Resistance

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 Person Obtaining Consent and Authorization	Signature of Person Obtaining Consent and Authorization	Date	Time (AM / PM)

☐Consent and authorization were 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: _____