Lifestyle Intervention plus Metformin to Treat Frailty in Older Veterans with Obesity

NCT04221750

September 13, 2024

Department of Veterans Affairs

VA RESEARCH CONSENT FORM

Subject Name: _____ **Date:** _____

Subject Initials: _____

Principal Investigator: DENNIS VILLAREAL **VAMC:** _____

H-46970 - LIFESTYLE INTERVENTION PLUS METFORMIN TO TREAT FRAILTY IN OLDER VETERANS WITH OBESITY

Consent Form

Concise and Focused Presentation

This study plans to learn whether metformin (study pill) adds to the beneficial effects of six months of lifestyle therapy (weight loss and exercise training) on physical function and well-being in older adults with obesity. Animal studies have shown that metformin improves health span (the part of a person's life during which they are in good health) and increases life expectancy. We will be measuring your physical function, muscle mass and strength, bone mass and strength, markers of muscle and bone function, and well-being while you undergo weight loss by diet and exercise training during the study period.

The benefits of participation include potential health improvements from the weight loss and exercise training such as on physical function, risk for heart disease, memory, thinking, mood, and well-being. You may also experience benefits from metformin such as decreasing your risk for diabetes and added benefits to weight loss and exercise. The risks include musculoskeletal injuries and disturbances in heart rhythm (rare) during exercise, pain, bleeding, or infection from blood draws and muscle studies, exposure to radiation, and possible loss of confidentiality. Risks associated with metformin include but not limited to nausea and diarrhea which are usually temporary. Alternative to participation is seeking weight loss independent of the study by enrolling in the MOVE (Managing obese/overweight veterans) program or at a commercial weight loss program (for example, Weight Watchers). You may also enroll in a health club for exercise training. You may also receive metformin through your regular doctor.

Your participation in the study is purely voluntary.

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study.

Obesity is becoming common in older adults, including many older veterans and has become a major concern. In older adults, obesity worsens the age-related decline in physical function resulting in frailty, decrease in quality of life, loss of independence, and increase in nursing home admissions. Weight loss from lifestyle therapy improves physical function and improves frailty. However, improvement in physical function is modest at best and most obese older adults remain frail. There are concerns that the weight loss could worsen the underlying age-associated loss of muscle mass and strength; and reduced bone mass in frail obese elderly. Because weight loss may have potential harmful effects in the older population, the appropriate clinical approach to obesity in the elderly remains controversial.

Metformin is a widely available drug used in the treatment of diabetes. Studies show that metformin may improve health span and increase lifespan, reduce frailty and minimize decline in muscle mass.

This research study is sponsored by Department of Veterans Affairs, Office of Research and Development

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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.

Purpose

To determine the effects of lifestyle therapy (weight loss and exercise) plus metformin on physical function, muscle, bone, fat, and perceived well-being in older veterans with obesity.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine and Michael E. DeBakey Veterans Affairs Medical Center.
The total number of subjects to be recruited is 114. The expected duration of your participation across the course of your entire participation time is ~ 8 months.

A. SCREENING TESTS - to determine whether you are eligible to participate you will undergo a medical history, physical examination, blood tests, physical function tests (see below), DXA (bone scan, a machine that uses a low dose of x-ray), electrocardiogram (EKG, a machine that records the activity of your heart), and graded exercise test. The purpose of the graded exercise test is to determine the health of your heart and will require you to exercise for approximately 10-15 minutes until you reach a point of fatigue. It will take approximately a total of 120 minutes to complete the screening tests.

B. BASELINE AND FOLLOW-UP TESTS - if you are eligible to participate and choose to do so, you will undergo a series of tests and procedures. It will take approximately a total of 135 minutes to complete the baseline tests, 60 minutes to complete the follow-up tests at 3 months, and 180 minutes to complete the follow-up tests at 6 months.

a. Body Composition assessments

Dual energy x-ray absorptiometry (DXA). The amount of fat, muscle, and bone in your body will be measured by DXA (a machine that uses a low dose of x-ray). This test involves lying on a table and having your body scanned by the machine for about 30 mins.

Magnetic resonance imaging (MRI). Fat and muscle in your thighs will be measured by MRI. During the MRI examination, you will lie on a table confined to a small space inside a cylindrical machine which uses magnetic fields and radio waves to take special pictures. In order to obtain good pictures, it is important that you do not move during the procedure. At certain times, you will be asked to slowly and carefully change your position on the MRI bed while a technician monitors you for safety. The examination will last about 30 minutes.

High resolution quantitative computed tomography (HR-pQCT). This machine is able to assess the amount, thickness, and arrangement of bone that determines the strength of bone in your leg and forearm. During the examination, you will sit down on a chair in front of the machine. You will be asked to extend one of your legs (usually the left) and one of your forearm (usually the left) inside a cylindrical

machine which uses X-rays to take special pictures. In order to obtain good pictures, it is important that you do not move during the procedure. The examination will last approximately 15 min.

Waist circumference will be measured with a tape measure

DXA will be done at baseline, 3 months, and 6 months. HR-pQCT will be done at baseline and 6 months.

MRI will be done at baseline and 6 months.

b. Blood tests. Blood (~5-6 tablespoons) will be drawn for routine chemistries (blood count and electrolytes), blood sugar, cholesterol, hormones, and markers of bone function and inflammation. These tests will be performed at baseline and after 3 and 6 months. Blood samples will be banked for future use.

c. Urine Sample Collection - to measure different biomarkers of aging. The tests will be done at baseline, 3 months and 6 months. Urine samples will be banked for future use.

d. Physical function tests: The Physical Performance Test will evaluate your ability to do activities such as walking, climbing steps, and picking up small objects such as a coin. Each item of the physical performance test is scored on a scale of 0 (worse) to 4 (best). Strength will be tested by having you use your arms or legs to push and pull as hard as possible against a special machine. Endurance will be measured by how quickly and how far you can walk within a specific amount of time. These tests will be done at baseline and after 3-months and 6 months.

e. Questionnaires: It will take approximately 60 minutes each time to complete all questionnaires. The SF-36 will ask you how you feel about your quality of life. The Functional Status Questionnaire will ask about things that we all need to do as a part of our daily lives. The Impact of Weight on Quality of Life Questionnaire-Lite will evaluate the effect of excess weight on your quality of life. The psychometric tests and mood scale will assess your cognition (memory and thinking) and mood. The St. George's Respiratory Questionnaire will ask you about respiratory symptoms that may affect your quality of life. The physical activity questionnaire will evaluate your level of physical activity. You will also be asked to wear accelerometers (a small piece of equipment that measures your level of physical activity) for 7 days. These will be completed at baseline and at the end of the study.

f. Measurement of aerobic capacity: You will be asked to walk on a treadmill while breathing through a mouthpiece, and the amount of oxygen you consume will be measured. This test evaluates the ability of your heart to provide your muscles with oxygen. This test will be performed at baseline and at the end of the study.

g. Measurement of lung function. You will be asked to take a deep breath in and blow your breath out as hard and fast as you can into a machine for at least 6 seconds. The machine measures the amount of air you can blow out and how fast you can blow it out. We have you do this 3 or more times so we can get an accurate measure of your lung function. This test will be performed at baseline and at the end of the study.

h. Diet evaluation: You will meet with a dietitian for about ½ hour. The dietitian will ask you to measure and write down everything that you eat and drink for 3 days. At the end of the 3 days, you will meet with the dietitian again to review your food diary. This will be done at baseline, 3 months and at the end of

the study.

i. Stool collection. A stool sample will be collected to determine whether weight loss and exercise plus metformin (study pill) change the types of bacteria (germs) that are normally present in your large intestine (bowel). You will be given a stool collection kit with detailed instructions and collection tools needed. This will be done at baseline and at the end of the study.

MUSCLE AND FAT STUDIES: These tests are optional and are not required in order to take part in the overall study. These tests will be done at baseline and after 6 months.

We will obtain biopsy samples of muscle tissue from your thigh. This involves numbing your skin with local anesthesia (by injecting 2% xylocaine), making a small (approx. the size of the dotted line ------; ½ cm) incision on the thigh for the muscle biopsy, removing a small (approx. 1/15th of an ounce) piece of muscle tissue. During the muscle biopsy, fat within and around the muscle may also be obtained. The incision is then closed with a piece of sterile tape. We will also obtain biopsy samples of fat tissue underneath the skin of the abdominal wall near your navel. This will also involve numbing your skin with local anesthesia (by injecting 2% xylocaine), making a small (approx. the size of the dotted line ------; ½ cm) incision on the abdomen, removing a small (approx. 1/15th of an ounce) of fat tissue using a liposuction needle under sterile conditions. The incision is then closed with a piece of sterile paper. The tissue samples will be banked for future use.

I agree to have the muscle and fat biopsy studies: Initial _____ Date_____

Risks of muscle and fat biopsies: The risks include discomfort, bleeding, bruising, temporary numbness or loss of sensation in the skin in the region of biopsy (<2%), and scarring. Occasionally some people experience dizziness or feel faint. Risks associated with the injection of the local anesthesia are an allergic reaction (redness and swelling of the skin in the area of the injection, red bumps onthe body, and in very rare instances, difficulty in breathing, low blood pressure and death). The anesthesia is the same as the local anesthesia used by most dentists. If you have not experienced an adverse reaction from anesthesia received at the dentist s office, it is unlikely for you to have allergic reaction. An infection can occur at the biopsy site. Careful, sterile techniques are used when obtaining samples to decrease the risk of infection. Biopsies may be associated with the formation of blood clots.

SUMMARY OF ASSESSMENTS AT EACH STUDY VISIT

SCREENING VISIT
Informed consent
Blood tests

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Medical history
Physical examination
DXA scan
Electrocardiogram
Graded exercise test

BASELINE VISIT
MRI
HR-pQCT
Waist circumference
Blood tests
Physical function tests
Questionnaires
Aerobic capacity
Lung function test
Diet evaluation
Urine sample collection
Stool sample collection
Muscle and fat biopsy (optional)

MONTH 3 VISIT
DXA scan
Blood tests
Physical Function Tests
Diet evaluation
Urine sample collection

MONTH 6 VISIT/End of Study procedures
Physical examination
MRI
HR-pQCT
Waist circumference
Blood tests
Physical function tests
Questionnaires
Aerobic capacity
Lung function test
Diet evaluation
Urine sample collection

Stool sample collection
Muscle and fat biopsy (optional)

C. INTERVENTIONS

After the medical screening and baseline assessments are complete, you will be randomly assigned (like a flip of a coin) to receive either:

1) Group 1: Lifestyle therapy (weight loss and exercise) + study pill. If you are randomly assigned to this group, you will be asked to participate in a weight management program and exercise training program. You will receive, under the care of a research dietitian, a special diet and attend group behavior modification sessions lead by the dietitian. These sessions will include classes on topics such as keeping track of what you eat, using food diaries, stress management, problem-solving, social support, changing problem behaviors, and identifying reasons or cues for eating. These sessions will last 75-90 min, which will be held weekly. You will be asked to lose at least 10% of your body weight during the intervention. In addition, you will participate in the exercise training sessions on 3 nonconsecutive days for approximately 60-90 minutes at our exercise facility. Each session will be led by an exercise trainer and will include exercise to improve flexibility, strength, endurance, and balance.

2) Group 2: Healthy lifestyle + study pill. If you are randomly assigned to this group, you will be asked to attend/participate in a monthly meeting to discuss some very general healthy lifestyle topics. Group sessions will include education classes focused on diet/nutrition, exercise, and social support. You will undergo the above series of assessments as indicated. You will be given the results of the tests that you complete, so that you may learn more about your health.

All groups will receive the study pill. The study pill could be metformin or placebo. A placebo is a pill that looks like medicine but is not real. It will have no medical effect on you. The study pill will be initiated at a dose of 500 mg (one tablet) orally once a day with meals. After a week, the dose will be increased to 1000 mg (two tablets) daily. After another week, the dose will be increased to 1500 mg (three tablets) daily. If gastrointestinal symptoms (e.g. nausea, diarrhea) appear as the dose is advanced, the dose will be decreased to the previous lower dose and the dose will be advanced at a later time. To monitor any necessary adjustment in dose, one of the study doctors will know if you are on the drug or the placebo, but neither you nor the rest of the study team will know which medication you are taking as they are identical in appearance. However, this information is available in case of an emergency. You will continue to take this medication for up to 6 months.

Because chance decides which group you will be in, the intervention you receive as part of this study may not be what your own doctor would choose for you.

You will be given a multivitamin and calcium supplementation to take daily by mouth.

During the COVID pandemic, participants may also receive their behavioral diet therapy through phone calls or telehealth at home, while they will be instructed on performing their exercises at home.

BIOLOGICAL SPECIMENS AND STORAGE OF TISSUE FOR FUTURE USE

Researchers for this study will collect samples of blood and urine for analyses which we are requiring you to provide to participate in this study. The investigators would also like to collect muscle and fat tissue samples (optional). These samples may be sent to other laboratories for specialized procedures and equipment. If you agree, any leftover blood, urine and tissue samples will be kept and may be used for future research to learn more about the effects of lifestyle intervention plus metformin. Any study using your samples must also be approved by an Institutional Review Board. The research that is done with your blood and optional urine and tissue samples is not designed to specifically help you. It might help researchers understand the effects of lifestyle intervention plus metformin in humans when new research techniques become available. Reports of research that is done with your samples will not be given to you or your doctor. These reports will not be put in your records. The research using your blood, urine and optional tissue samples will not affect your care.

It is your choice whether to allow the study investigators to keep your blood, urine and optional tissue samples for further research. No matter what you decide to do, it will not affect your care. If you decide now that your blood, urine and optional tissue samples can be kept for research, you can change your mind at any time. Just inform the study coordinator and let him/her know that you do not want the investigators to use your blood. urine and optional tissue samples, and they will no longer be used for research. Otherwise, they will be stored for up to 10 years, or until they are used up.

In the future, people who do research with your blood, urine and optional tissue samples and people who do other types of health related research may need to know more about your health. While the investigators may give these researchers reports about your health, they will not give your name, address, phone number or any other information that will let the researchers know who you are. The results of the research done on your samples will not be told to you and will not be put in your health records. You will not hear from us unless we find information that may have an impact to your health.

Your blood, urine and optional tissue samples will not be sold. The research done with your samples may help develop new products in the future, but there is no plan to pay you.

The possible benefits of research from your blood, urine and optional tissue samples include learning more about the effects of lifestyle intervention plus metformin on frailty and aging and related diseases, how to prevent them and how to treat them. The greatest risk in storing your samples is the release of information from your health records. Information that may easily identify you will be kept private. The chance that these information will be given to someone else is very small. There will be no cost to you for any blood and optional urine and tissue sample collected and stored by the investigators.

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Please read each question below and think about your choice. After reading each question, circle "Yes" or "No". If you have any questions, please talk to a member of the research team. No matter what you decide about the storage and use of your samples, you may still take part in the study.

1. Investigators outside of this study may be allowed to use my blood, urine and optional tissue samples for future research to learn more about the effects of lifestyle intervention plus metformin.

Your samples will be stored in a freezer for up to 10 years at the Michael DeBakey VA Medical Center facility and VA Science and Health Initiative to Combat Infectious and Emerging Life-Threatening Diseases (VA SHIELD) repository for future related research.

YES NO Subject's Initial's: _____

2. Only investigators within this study may be allowed to use my blood, urine and optional tissue samples for future research regarding the response to lifestyle intervention plus metformin.

Your samples will be stored in a freezer for up to 10 years at the Michael DeBakey VA Medical Center facility and VA Science and Health Initiative to Combat Infectious and Emerging Life-Threatening Diseases (VA SHIELD) repository for future related research.

YES NO Subject's Initials: _____

Clinically Relevant Research Results

The comprehensive medical screening to evaluate your eligibility in the study may discover abnormal findings in blood tests, bone scan, and electrocardiogram. You will be provided a copy of these tests and referred to your primary care physician for further evaluation and appropriate treatment.

Sharing and Future Research Studies with Identifiable Private Information

Information that identifies you may be removed from your identifiable private information collected as part of this research, and after such removal, your information may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

Sharing and Future Research Studies with Identifiable Biospecimens

Information that identifies you may be removed from your identifiable biospecimens collected as part of this research, and after such removal, your biospecimens may be used for future research studies or distributed to another investigator for future research studies without additional consent/authorization from you.

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Confidentiality

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Full Social Security #
- Partial Social Security # (Last four digits)
- Identifiable biospecimens

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts

You may have side effects while on the study. Everyone taking part in the study will be followed carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your study doctor may give you medicines to help lessen the side effects . In some cases, side effects can be serious, long lasting, or may never go away. There is also a risk of death. Many side effects go away soon after you stop taking metformin.

You should report to your study doctor any side effects you experience while taking part in the study .

Randomization risks:

o You will be assigned to a treatment program by chance, and the treatment you receive may prove to be less effective or to have more side effects than the other study treatment (s) or other available treatments.

Risks and side effects related to metformin are listed below:

o Frequent (Greater than 20%). Side effects include: nausea and/or vomiting and diarrhea. These side-effects are usually temporary and lessen over a few weeks time, eventually going away on their

own.

o Occasional (Between 2-20%). Side effects include: headaches, dizziness and/or light headedness.

o Rare (Less than 2%). Side effects include: Low blood sugar does not occur under usual circumstances of use, but could occur when caloric intake is deficient, or during concomitant use of other glucose-lowering drugs. Lactic acidosis (build up of acids in the body) is a very rare side- effect which usually occurs when there are possible risk factors such as kidney or liver impairment, use of x-ray contrast agents, or excess alcohol intake.

Allergic reaction: With any drug there is a risk of allergic reaction. Symptoms may include but not be limited to trouble breathing, fast heart rate, rash, dizziness, and swelling. If you experience any of these symptoms, you should contact your study doctor immediately.

Risks associated with testing procedures and lifestyle interventions
o Frequent (Greater than 20%)
- This research involves exposure to radiation from three dual energy x-ray absorptiometry (DXA) scans and two HR-pQCT scans for bone and body composition measurements. We are exposed to radiation every day of our lives from both natural and manmade sources. The average effective dose to a member of the U.S. from these sources is approximately 360 millirem per year. By comparison, the radiation dose that you will receive when participating in this research study is less than the annual amount and the risk of potential harmful effects is considered to be minimal.
- Possible side effects of blood drawing and a thin tube inserted through your vein are discomfort , bruising, and /or bleeding at the site of the needle.
- Feeling fatigue while exercising. You will be allowed to rest if necessary and request to stop this exercise if you are tired.
- There is a risk of a small amount of muscle and bone density loss associated with weight loss, however, researchers don t know whether this has any long-term harmful effects (when combined with exercise training) since physical function may improve.

o Rare (Less than 2%)
- An infection can occur at the site of the vein insertion for blood draw; however, careful sterile technique is used to decrease this risk. Occasionally, some people may experience dizziness after blood drawing.
-The risk of participating in an exercise program includes fractures, sprains, falls, tendon injury, and sore muscles, and joints on different parts of the body. However, these complications will be minimized as you will be doing warm-up and cool-down exercises and you will receive close monitoring to reduce the risk of these complications.
- Exercise training and testing is associated with a slight risk of developing serious disturbances in

heart rhythm, temporary drop in blood pressure, or, very rarely, heart attack and death. Disturbances in heart rhythm are typically reversible. A physician willbe available should a medical emergency arise.
- The risks of muscle and fat biopsies include discomfort, bleeding, bruising, temporary numbness or loss of sensation in the skin in the region of biopsy, and scarring. Occasionally some people experience dizziness or feel faint. Risks associated with the injection of the local anesthesia are an allergic reaction (redness and swelling of the skin in the area of the injection, red bumps on the body, and in very rare instances, difficulty in breathing, low blood pressure and death). The anesthesia is the same as the local anesthesia used by most dentists. If you have not experienced an adverse reaction from anesthesia received at the dentist office, it is unlikely for you to have allergic reaction. An infection can occur at the biopsy site. Careful, sterile techniques are used when obtaining samples to decrease the risk of infection. Biopsies may be associated with the formation of blood clots.
-Another rare risk of weight loss is the formation of gallstones (a hard mass in the organ next to your liver where the body stores a liquid called bile).
- When blowing out forcefully during the lung function testing or when having blood drawn, you may become lightheaded, develop a headache, or feel warm. In rare case of lightheadedness, you may even temporarily pass out. If you start becoming lightheaded or feel otherwise unwell during lung function testing, please tell the staff immediately.
- Risks associated with fecal sample collection include: experiencing emotional stress related to working with your own feces. Mishandling the sample can lead to infections, however, personal protection equipment will be provided, and safe hand washing technique will be taught to reduce the risk to only rare cases.

There are risks of stress, emotional distress, inconvenience and possible loss of privacy and confidentiality.

For more information about risks and side effects, ask your study doctor.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

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Potential Benefits

The benefits of participating in this study may be: potential health improvements from the weight loss and exercise intervention such as in physical function, risk for heart disease, memory, thinking, mood, and well-being. You may also experience benefits from the study drug (metformin) such as decreasing your risk for diabetes and added benefits to weight loss and exercise including improving physical function and helping to preserve muscle and bone during dieting.

Obesity in older adults, including many aging veterans, is a major public health problem. In fact, the public health success that has occurred in recent years could be in danger if lifestyles of older adults are neglected. The novel health outcomes and mechanistic-based data generated from this study will have important ramifications for the standard of care for this rapidly increasing segment of the aging veteran population. The results could be incorporated in the MOVE (Managing Overweight/Obese Veterans) program, which currently does not have any guidelines for eligible veterans if they are 70 years or older.. However, you may receive no benefit from participating.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: Other than not taking part in the research, you may choose to speak with your doctor about what is the best treatment for you. You may receive metformin without participating in the study through your regular doctor. In addition, you may seek weight loss independent of the study by enrolling in the MOVE (Managing obese/overweight veterans) or at a commercial weight loss program (for example, Weight Watchers). You may also enroll in a health club for physical training..

Subject Withdrawal from a Study

Your participation in this study is completely voluntary. You may withdraw from the study by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. Your choice will not at any time affect the commitment of your health care providers to administer care. There will be no penalty or loss of benefits to which you are otherwise entitled.

Investigator Withdrawal of Subject from a Study

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication or unable to complete 80% of the weight loss and/or exercise classes) or because the entire study is stopped. The sponsor, investigator, Food and Drug Administration, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

In return for your time and the inconvenience of participating in this study, you will be paid $50 for

completing all the baseline testing, $50 for completing all midpoint testings (at 3 months) and $50 for completing all the final testing (at 6 months). In addition, if you agree to the optional muscle and fat studies, you will be paid $125.00 for both muscle and fat biopsies to be done at baseline and at the end of the study. Thus, the total amount you may receive if all of the procedures are completed is $400.00. You will receive the payment approximately (3) weeks after the study visit has been completed. You will receive the payment via direct deposit to your bank account within approximately 5 days after your completion of the baseline, midpoint, final testing, or muscle studies.

Research Related Injury

In the event of illness or injury, you may contact Dr. Denis Villareal, the principal investigator, during the dat at (713)578-4300 or (713)794-7156 (phone) or (713)794-7134 ext 2015(beeper) after office hours. You may also contact the Michael DeBakey VA Medical Center Emergency Department (713)791-1414 ext 27440 or ext 23748 for emergencies only.

Every reasonable safety measure will be used to protect your well-being. If you are injured as a result of taking part in the study, the VA will not provide financial compensation but will provide necessary medical

treatment at no cost to you unless the injury was due to your not following the study procedures. Furthermore, medical treatment for injury related study procedures may include hospitalization, emergency room visits, or additional radiology studies, blood draws, emergency treatments, and specialty specific physician needed to address the task at hand. If any medical problems occur in connection with this study, the Michael DeBakey VA Medical Center will provide both emergency care and ongoing care for any research-related injury. You do not give up any of your legal rights and you do not release the Baylor College of Medicine or VA from any liability by signing this form.

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Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, DENNIS VILLAREAL, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: DENNIS VILLAREAL at (713) 578-4300 or (713) 794-7156 (phone) during the day and 713-794-7134 ext 2015 (beeper) after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.
Under Federal Regulations, the VA Medical facility shall provide necessary medical treatment to you as a research subject injured as a result by participation in a research project approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees. This requirement does not apply to treatment for injuries that result from non-compliance by a research subject with study procedures. If you sustain an injury as a direct result of your study participation, medical care will be provided by the Michael E. DeBakey VA Medical Center. The Department of Veterans Affairs does not normally provide any other form of compensation for injury. You do not waive any liability rights for personal injury by signing this form.

You may withdraw from this study at any time without penalty or loss of VA or other benefits to which you are entitled. Your participation will not affect the way you now pay for medical care at the VAMC. If you would like to verify the validity of the study and authorized contacts, you may speak with the Michael E. DeBakey Veterans Affairs Medical Center Research Office at 713-794-7918 or 713-794-7566.

Department of Veterans Affairs

VA RESEARCH CONSENT FORM

Subject Name: _____ **Date:** _____

Subject Initials: _____

Principal Investigator: DENNIS VILLAREAL **VAMC:** _____

H-46970 - LIFESTYLE INTERVENTION PLUS METFORMIN TO TREAT FRAILTY IN OLDER VETERANS WITH OBESITY

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness	Date