

**THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER and THE WEATHERHEAD
CENTER FOR PREVENTING AND REVERSING CORONARY DISEASE - HOUSTON**

Randomized Trial of Comprehensive Lifestyle Modification, Optimal Pharmacological Treatment and PET Imaging for Detection and Management of Stable Coronary Artery Disease

The CENTURY Trial

HSC-MS-08-0312

INFORMED CONSENT FOR RESEARCH STUDY

INVITATION TO TAKE PART

You are being invited to take part in a research project called “Randomized Trial of Comprehensive Lifestyle Modification, Optimal Pharmacological Treatment and PET Imaging for Detection and Management of Stable Coronary Artery Disease: **The CENTURY Trial**” conducted by K. Lance Gould, MD and S. Sdringola, MD and research staff at the University of Texas Health Science Center at Houston and Memorial Hermann Hospital Texas Medical Center. Your decision to take part is voluntary and you may refuse to take part, or choose to stop taking part, at any time. A decision not to take part or to stop being a part of the research project will not change the services that are available to you from your own regular physicians or Memorial Hermann Hospital Texas Medical Center. You may refuse to answer any questions asked or written on any forms. This research project has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston as Protocol Number: (HSC-MS-08-0312). Please take your time to make a decision, and discuss this proposal with your personal doctor, family members, and friends if you wish. The principal investigator, Dr. Gould, and the research staff will be glad to answer any questions regarding the study at any time in person or by calling a 24 hour phone number (713 500-6611).

DESCRIPTION OF RESEARCH

Purpose of the Study

Your doctor may have ordered a stress test because you have coronary artery disease (CAD) or you are at risk for this disease. CAD is caused by buildup of cholesterol deposits in the lining of the walls of the blood vessels that supply blood to the heart muscle. This process is called atherosclerosis and may lead to heart attack and/or death without any warning signs.

The **main purpose** of this study is to compare current standard therapy to a comprehensive therapy program utilizing PET (Positron Emission Tomography) rest and stress test together with encouraging a healthy lifestyle and targeting risk factors for coronary artery disease.

This study will compare patients assigned to “optimal standard therapy” (= usual current medical care strategy) or to “ PET + comprehensive therapy” (=experimental medical care strategy).

The comprehensive therapy program is meant to support and not to substitute the care provided by your doctor.

PROCEDURES

You are being invited to take part in this research study because your primary care doctor has requested that you have a SPECT stress test or you have risk factors for heart disease. The results of the SPECT study as ordered by your doctor will be released to you and your physician. Your physician will decide if you need any further treatment based on the results of the SPECT stress test.

If you decide to take part in the CENTURY Trial a PET scan will be scheduled within 2 weeks. You will be randomly assigned (50/50 chance like the flip of a coin) to the group having the PET scan results released immediately or at the end of the study. At the same time you will be randomly assigned to the group who will either undergo a comprehensive risk factor modification program or a standard therapy group.

If you are assigned to the comprehensive therapy group, during each visit you will meet with the CENTURY study team. The CENTURY study team includes a physician, a nurse, a dietitian, an exercise physiologist or physician in this role. At each visit the nurse will review your health status, current medicines, and measure weight, blood pressure, and body fat measurements. Annually, you will have a physical exam, and receive consultation and instructions from a dietitian. You will be asked to complete and turn in a 3-day food/drink diary before each planned visit. A doctor will review the information with you and give you final recommendations about exercise and toward your progress. A regular treadmill stress test will be performed every year to assess your physical fitness. A total of 14 clinic visits are planned during the 5 years of the study (baseline, month 1, 2, 4, 8, 12 and then every 6 months or more often if needed for optimal risk factor modification.

If you are assigned to the standard therapy group, at each visit the nurse will review your health status, current medicines, and measure weight and blood pressure. You will have a physical exam, and receive a consultation from a dietitian. You will be asked to complete and turn in a 3 day food/drink diary before each visit. A doctor will review the information with you and give you final recommendations toward your progress. You will have a total of 5 clinic visits over the 5 years of the study (one visit every 12 months). A study research nurse or representative may contact you every 4 to 6 months by telephone, mail or protected e-mail for a short interview to follow your health status.

The participants of both groups will have a rest-stress and gated PET study at baseline, year 2 and year 5 or additionally offered as indicated below. The PET scan measures the blood flow in your heart muscle and the gated cardiac images measure how well your heart is pumping blood to your body. You will be asked to refrain from all caffeine for at least 24 hours before the PET scan.

At the same time you will have an exercise treadmill stress test to see what your fitness level is, a review of the quality of your diet based on your food diary, and blood work that includes basic chemistry levels, your cholesterol levels in detail and caffeine level. You will have about 5 tablespoons of blood drawn from a vein in your arm at baseline, year two and year five. In addition, a sample of your blood will be saved indefinitely for future cardiovascular risk factor analysis.

All the above procedures are NOT experimental but you might not ordinarily receive them unless you are taking part in this study. Because we are evaluating the effectiveness of the PET scan results in managing patient care, the standard therapy group PET scan results will not be given to you until the end of the study. Finally participants of both groups undergoing a revascularization procedure to improve blood flow to the heart muscle, such as coronary balloon dilatation or bypass surgery – as determined by you and your doctor - will be offered an additional at no cost PET study that you can use to compare to your baseline and see how much you have improved after the procedure. We

are ethically obligated to offer to repeat the PET scan if caffeine is detected in your blood work since caffeine affects blood flow during stress imaging and could affect the PET scan results or for technical imaging issues.

The participants of both groups will be asked at the time of their yearly visit to fill out 3 short questionnaires (taking a total of 20 minutes) to collect data on how you use the resources available to you and self health assessment. This information is necessary for our economic analysis so we can measure which treatment group is most cost-effective.

Also as part of the economic analysis, billing records from any cardiovascular related service or event will be collected from your hospital or your primary care physician.

You will continue your regular follow-up visits with your primary care physician. He/She will still be in charge of your healthcare even though you are taking part in this research study.

TIME COMMITMENT

Yearly study visits will take about 2-3 and 1/2 hours for both groups (up to 4 ½ hours for PET scan visits) and about 1 and 1/2 hour for the comprehensive therapy group interim visits. The PET scan takes up to about 2 hours and the treadmill exercise test takes about 30 minutes. The study duration is 5 years. Those assigned to the comprehensive therapy group will be asked to return 5 times during the first year and 2 times each of the remaining four years of the study. Those assigned to the standard therapy group will be asked to return each year and will receive a follow up phone call every 4 to 6 months.

RISK and/or DISCOMFORTS

The comprehensive therapy program is trying to achieve the best possible control of known coronary artery disease risk factors. This will be done by using what is currently recommended for healthy lifestyle and cholesterol lowering medicine. Therefore, if you are assigned to the comprehensive therapy group you should not be at increased risk, compared to the standard therapy group.

Every patient entering the trial, will have a PET study and a treadmill stress test. All the study patients will have a PET study and treadmill stress test at the first visit, 2 years and 5 years. This is not current standard of care and may represent a potential radiation risk. The comprehensive therapy group will have a treadmill exercise stress test every year.

The PET scan requires the placement of a small, short plastic tube (I.V. catheter) into an arm vein in order for the radioactive substance and stress drug to be given. The insertion of the standard intravenous tube may create a small amount of pain or discomfort like drawing blood.

The stress medicine, dipyridamole, was first developed by the principal investigator (Dr. K. Lance Gould) for imaging blood flow in the heart muscle. It is approved by the FDA and has been safely used in millions of patients in most countries. Common side effects are headache (12%), dizziness (11%) or nausea (4%). These symptoms are mild and are usually gone by the end of the study. In patients with coronary heart disease, 19% may develop chest pain. If chest pain should develop due to unexpected coronary artery disease, the dipyridamole stress is stopped by giving an antidote (aminophylline) through the IV catheter to stop the effect of the dipyridamole within 30 seconds. All subjects are closely monitored by blood pressure, continuous ECG monitoring with a cardiologist present throughout the study. For over 9000 cases of dipyridamole stress PET imaging done personally by the principle investigator, there have been no deaths, strokes or major injury due to the dipyridamole PET test. If dipyridamole cannot be used, alternatively, another approved stress medicine,

adenosine, will be used. It has been widely used as a first choice or alternative to dipyridamole for nuclear stress testing. Adenosine is safe and may produce similar side effects as dipyridamole but its effects lasts a few seconds and it is much less likely to require aminophylline to reverse any side effects.

The amount of radiation you will receive is relatively low. The average yearly background radiation dose to everyone is 3mSv per year. The total radiation dose to someone undergoing a single rest-stress and gated cardiac PET-CT is approximately 3.7 to 4 times this background radiation. The radiation dose to the kidneys from the radioisotopes (for example: rubidium-82, nitrogen-13 ammonia, copper-62, fluoride-18 flurpiridaz) is about the same dose to the kidneys received from other scans of the kidneys or abdomen. None of these low dose levels are associated with increased levels of cancer or other adverse effects. There will be a total of 3 scheduled PET scans done over a 5 year interval and potentially additional PET scans if you undergo a heart balloon, stent or bypass procedure, if caffeine is detected in your blood work, or for technical imaging issues as mentioned earlier in this consent.

Pregnant women should not have this test because of unknown or immeasurable potential risk to a developing fetus.

The Exercise Treadmill Test is used to assess your exercise tolerance (fitness) and will increase your heart rate and blood pressure. It will not be done if for any reason you are unable to exercise. The risk of the stress portion of the test is very small and similar to what you would expect from any strenuous form of exercise (jogging in your neighborhood, running up a flight of stairs, etc.). Experienced medical staff is in attendance to manage the rare complications like sustained irregular heart beats, unrelieved chest pain or heart attack.

BENEFITS

Subjects taking part in the CENTURY trial could benefit from having electrocardiograms, exercise treadmill stress tests, diet evaluations and complete blood work of your cholesterol profile at no cost. The results of these tests will be given to you and your primary care physician.

The benefit for the society could be the discovery of a more efficient and cost-effective way of practicing medicine and diagnosing coronary artery disease. The results of this study could demonstrate the healing power of an educated and motivated patient over expensive pills and procedures which do not substitute for proper diet and exercise.

Finally, taking part in this study may help patients with risk factors or with established CAD to get better care in the future.

ALTERNATIVES

Taking part in this study is entirely voluntary. The alternative to taking part in this study is to not to take part or to withdraw from the study at any time.

Diet and exercise physiology assessment and recommendations from qualified professionals are available if clinically indicated but usually not covered or only partially covered by health insurances, particularly for continued periods of treatment.

STUDY WITHDRAWAL

Your taking part in this study is voluntary. You may withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled, If you decide not to take

part in this study or withdraw from the treatment phase before study completion, you may be asked to complete the end-of-study evaluations.

Under certain circumstances, the investigator may stop your taking part in the study without your consent. The reasons include: failing to cooperate fully with the conduct of the study, your development of a serious unrelated illness, or if the principal investigator decides to cancel the study. You will be told if new information is received that may change your willingness to take part in this study

You have the option to be contacted if clinically relevant information is developed over time. I **DO** _____ / **DO NOT** _____ want to be contacted if relevant information is developed over time .
(initials) (initials)

IN CASE OF INJURY

If you suffer any injury as a result of taking part in this research study due to the rest-stress PET scan procedure or treadmill stress test there is no provision for paying for your medical care by the University of Texas, by Memorial Hermann Hospital, Harris County Hospital District or by the principal investigator or his staff. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to K. Lance Gould, M.D. at 713-500-6611 and to the Committee for the Protection of Human Subjects at 713-500-7943.
You will not give up any of your legal rights by signing this consent form.

CONFIDENTIALITY

What is in place to assure the subject's confidentiality?

Please understand that representatives of the Food and Drug Administration (FDA) and/or the Committee for the Protection of Human Subjects (CPHS) may review your research and/or medical records for the purposes of verifying research data. The appropriate research staff of this project and FDA representatives can see personal identifiers in your medical records and in your clinical billing records. However, your identity will be shielded from the view of all unauthorized people. You will not be personally identified in any reports or publications that may result from this study. Any personal information about you that is gathered during this study will remain confidential to every extent of the law. A special number (or code) will be used to identify you on the lab work and diagnostic tests which are research to prevent you from getting charged or from others knowing you are taking part in this trial. There is a separate authorization form that you will be asked to sign that details the use and disclosure of your protected health information.

With your permission we will mail information regarding your lab work and diagnostic reports to your primary physician.

Yes, I give my permission to provide my lab and diagnostic reports to my primary care physician.

No, I do NOT give my permission to provide my lab and diagnostic reports to my primary care physician.

The additional blood sample will be identified by a study code and personal identifiers will be maintained securely. The samples will be securely stored at The University of Texas Health Science Center at Houston (UTHSC-H) and are the property of the Century Trial principal investigators and UTHSC-H. The principal investigators are responsible for the care and any

release of samples from the storage unit. Please be aware that if Dr. Sdringola or Dr. Gould leaves the University, the samples will remain the property of UTHSC-H. The results of any cardiovascular risk factor analysis will not be made known to you unless withholding the results will jeopardize your safety and well being, nor will the results be recorded in your medical records or released to any unauthorized third party.

If you decide to allow the additional blood sample, to be drawn you are providing your sample for use by the University of Texas Health Science Center at Houston , who owns any use of the results, treatments or inventions that can be made from the research. You will not be paid for any use of your samples or results.

Yes,_(initials)_____ I give my permission to provide an extra blood sample for future cardiovascular risk factor analysis.

No, (initials)_____ I do NOT give my permission to provide an extra blood sample for future cardiovascular risk factor analysis.

COSTS, REIMBURSEMENT, AND COMPENSATION

There is no direct compensation for taking part in this study. If you qualify and agree to take part you will receive the following free of charge; 3 PET scans, at least 3 electrocardiograms (EKG), at least 3 exercise stress tests, 3 complete sets of detailed analysis of blood lipids, as well as diet evaluations. For those in the comprehensive therapy group you will receive 14 diet and exercise physiology consults over the five years of the CENTURY study. You are not expected to incur any additional expenses due to your taking part in this study.

Parking and local public transportation fees (bus and train) will be reimbursed. If you receive a bill that you believe is related to your taking part in the research study, please contact Catey Carter, RN at 713-500-5200 with questions.

Follow up blood tests for those randomized into the Comprehensive Management Group (Stripes Group)

As part of intense risk factor modification to prevent and/or stabilize heart disease, the Century Health Study cardiologists may recommend a change or an addition to your cholesterol medications to reach target cholesterol levels for optimal lipid management. It is standard medical practice to have follow-up blood tests after adding or changing cholesterol medication to monitor the response of the medication as well as to monitor for any side effects of the medication.

Since these follow-up lab tests are a part of standard clinical medical practice, they are not reimbursed by the Century Health Study. The Century Health Study cardiologists will provide an order for the recommended lab tests as well as a diagnosis code. You or your health insurance is responsible for payment of these interim blood tests.

The Century Health Study provides three lab tests as part of the study at no charge to you at each PET scan visit: baseline, two and five years.

_____(initials) I understand that the costs of interim blood tests are not paid by the Century Health Study

QUESTIONS: If you have any questions please feel free to contact Dr. Lance Gould at (713)500-6611 or (713)500-5200.

SIGNATURES

Your participation is voluntary. You may choose not to participate or you may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled. There will not be any additional compensation for your participation in this study. Your employment will not be affected by your decision to participate or not participate in this research.

Taking part in this study is your choice. If you sign this form it means that you wish to take part in this research study. Sign below only if you understand the information given to you about the research and choose to take part. Make sure that any questions have been answered and that you understand the study. If you have any questions or concerns about your rights as a research subject, call the Committee for the Protection of Human Subjects at (713)500-7943. If you decide to take part in this research study, a copy of this signed consent form will be given to you.

Printed Name of Subject

Signature of Subject

Date

Time

Printed Name of Individual Obtaining Consent

Signature of Individual Obtaining Consent

Date

Time

CPHS STATEMENT:

This study (HSC-08-0312) has been reviewed by the Committee for the Protection of Human Subjects (CPHS) of the University of Texas Health Science Center at Houston. For any questions about research subject's rights, or to report a research-related injury, call the CPHS at (713) 500-7943.