ADULT CONSENT - CLINICAL BIOMEDICAL
Main Study Consent

Title of this Research Study

Invitation
You are invited to take part in this research study. You have a copy of the following, which is meant to help you decide whether or not to take part:

- Informed consent form
- "What Do I need to Know Before Being in a Research Study?"
- The Rights of Research Subjects

Why are you being asked to be in this research study?
You are being invited to take part in this study because:

- the results of your screening examination indicate you are eligible to participate (have low bone mass and blood tests were normal)
- you are 19 years old or older
- you have started menopause within the last 5 years
- you are not at high risk for fracture
- you weigh less than 300 lbs
- you are healthy

A total of 309 post-menopausal women will be enrolled in this study.

What is the reason for doing this research study?
There is a period of rapid bone loss in the first years after menopause. This makes women at high risk of developing osteoporosis and fractures. The purpose of the Heartland Osteoporosis Prevention study is to identify the best way to maintain healthy bones in the first years after menopause. The Heartland Osteoporosis Prevention study will compare the bone health of women who take calcium and vitamin D only to women taking calcium and vitamin D plus medication (risedronate) or exercise.

What will be done during this research study?
If you consent to participate in the study, you will be randomly assigned to one of three study treatment groups: 1) calcium and vitamin D supplements only, 2) calcium and vitamin D supplements plus medication to prevent bone loss (risedronate), or 3) calcium and vitamin D supplements plus exercise to prevent bone loss.

You will be asked to complete the following assessments at the time points indicated

below:

Assessments at Baseline:

1. pQCT (peripheral quantitative computed tomography): This is a CT scan to measure bone structure. The test will be completed on your lower leg in two areas. You will sit in a chair with your lower leg in the machine that assesses your bone. This will take approximately 15 minutes. The pQCT is performed for research only and the results have no value to your health care. Therefore, the results of these tests will not be sent to you or your healthcare provider.
2. Diet History: The investigators will calculate how much calcium you get from your diet. This will be used to prescribe the correct amount of calcium you need to get the recommended 1200 mg/day.
3. Medical History: Study personnel will interview you to get a complete medical history including medications and supplements that you take.
4. Self-Efficacy Questionnaires: You will fill out questionnaires related to your confidence in completing the interventions assigned to your study treatment group. For example if you are in the exercise group, the questionnaire asks about your confidence in performing exercise the number of times per week as prescribed. This information is used to inform the strategies used by the investigators to help you become more confident in your ability to manage the intervention.
5. Goal Setting Questionnaire: You will fill out questionnaires related to setting goals for completing the interventions assigned to your study treatment group. This information is used to inform the strategies used by the investigators to help you become more confident in your ability to manage the intervention.
6. Barrier Questionnaire: You only fill out this questionnaire if you are in the exercise group. It evaluates barriers to completing exercises, and your results help the investigators design strategies to make it easier for you to participate in exercise.
7. One Repetition Maximum (1 RM): If you are in the exercise group, your strength will be evaluated by performing a test which estimates the maximum amount of weight you can lift. This is used to prescribe weight loads for resistance training.

Assessments at 2 weeks:

1. You will be interviewed by study personnel to identify problems/issues with the study.

Assessments at 3 months:

1. If the vitamin D in your blood is very low or very high, you will be asked to

return at 3 months to have it checked again. If it is very high, we will also check your calcium and albumin at 3 months. If it is minimally low or normal, you do not have blood drawn.
2. You will complete the Self-Efficacy questionnaires and if you are in the exercise group, you complete the Barrier questionnaire.
3. You will complete the Goal-Setting questionnaire.
4. You will be interviewed by study personnel to identify problems/issues with the study.

If a blood test is not required, assessments at 3 months can be completed over the phone.

Assessments at 6 months:

1. You will complete a DXA (dual energy x-ray absorptiometry): This is a test to measure the bone density of your hip and back. You do not have to prepare for the test. You will lie on your back while the machine moves over you. The test will take about 30 minutes. Your results will be sent to your healthcare provider. In addition to bone density, investigators will calculate estimates of the strength of your bone using the DXA results. The results of these tests will not be sent to your provider because results have no use in the treatment of patients clinically.
2. You will complete a pQCT scan of your lower leg.
3. We will assess bone repair status. Bone is constantly breaking down and repairing itself. That is how it stays healthy and strong. Investigators will measure markers in your blood which indicate the status of this process. These tests are performed in the investigator's lab for research only and the results have no value to your health care. Therefore, the results of these tests will not be sent to you or your healthcare provider.
4. We will assess your vitamin D level. Your results will be sent to your healthcare provider.
5. The research exercise trainer will assess your 1 RM if you are in the exercise group.
6. Study personnel will complete a medical screening: blood pressure, height weight, waist circumference and document any changes in health or fractures.
7. You will complete questionnaires to document your regular physical activity patterns.
8. You will complete the Self-Efficacy questionnaires, and if you are in the exercise group, you complete the Barrier questionnaire.
9. You will complete the Goal-Setting questionnaires.
10. You will be interviewed by study personnel to identify problems/issues with

the study.

Assessments at 12 months (end of the study):

1. You will have a DXA, estimates of the strength of your bone, pQCT, and blood tests to evaluate your bone repair status. Results of the DXA will be sent to your healthcare provider.
2. Study personnel will complete a medical screening: blood pressure, height weight, waist circumference and document any changes in health or fractures.
3. You will complete questionnaires to document your regular physical activity patterns.
4. You will complete the Self-Efficacy questionnaires, and if you are in the exercise group, you complete the Barrier questionnaire.
5. You will be interviewed by study personnel to identify problems/issues with the study.

You will report any broken bones occurring during the study to the investigators when they happen.

INTERVENTIONS

At the first visit you will receive education on bone health and use of calcium and vitamin D supplements. You will be provided with medication cards with tablets in individual bubbles that are dated. This will help you to take the pills prescribed every day. You will be given "calcium" medication cards with the correct amount of calcium based on your diet history test. You will be given "vitamin D" medication cards that have tablets with the correct amount of vitamin D based on your blood test. Because calcium is best absorbed when taken without certain foods, you will be given instructions on the best way to take this supplement. You will return all medication cards with unused pills to the investigators every 4 weeks in the postage-paid, addressed envelopes provided.

Group Specific Interventions

All groups will take the calcium and vitamin D as described above. All groups will receive calcium and vitamin D supplements at three month intervals either in person, or via mail. Below describes additional, study treatment group specific interventions.

Group 1) calcium and vitamin D supplements only

At two weeks and 3 months study personnel will contact you to see how you are doing. The 3 month visit can be a phone call or face-to-face visit depending on how you are doing. If you have problems, study personnel will help you find ways to take the prescribed calcium and vitamin D.

You will return for 6 and 12 month assessments as described above.

Group 2) calcium and vitamin D supplements plus medication to prevent bone loss, "risedronate"
You will be prescribed risedronate, a medication that prevents bone loss, and it will be mailed to you shortly after your initial visit. Study personnel will also give you instructions for how to safely take this medication and help prevent side effects. The correct method is to take the risedronate with an 8 ounce glass of water, either upon arising in the morning or 2 hours after the last meal of the day. You are to remain upright and have no oral intake except water for at least 30 minutes after taking risedronate. Risedronate is to be taken once a month. You will receive your risedronate prescription at three month intervals, either in the mail or in person.

At two weeks and 3 months, study personnel will contact you to see how you are doing. The 3 month visit can be a phone call or face-to-face visit depending on how you are doing. You are asked to contact study personnel in the event of discomfort when taking this medication.
Study personnel will help you find ways to take the prescribed calcium, vitamin D and risedronate.
You will return for 6 and 12 month assessments as described above.

Group 3) calcium and vitamin D supplements plus exercise
In addition to taking calcium and vitamin D, the research exercise trainer (RET) will prescribe and teach you an exercise program to prevent bone loss. Exercises will then be completed at an Omaha metro area or Lincoln area YMCA of your choice or at the Salvation Army Kroc Center, at times of your choice, three times per week. Exercises will consist of weight lifting exercises and jogging with a weighted vest to stress the bones in your legs and back. Those with joint replacement of the hip and/or knee will complete "step-up" exercises instead of the jogging and leg press exercise machine. You will be provided with a detailed instruction manual and an exercise log which you complete each time you exercise. The exercise trainers at the YMCA or Kroc Center will be available upon request to assist and will review your progress every two weeks. From this information, trainers will instruct you on how to increase your exercises. The RET will also monitor your exercise logs and progress. She will schedule a visit if you are having problems with the exercises.
At two weeks and 3 months, study personnel will contact you to see how you are doing. The 3 month visit can be a phone call or face-to-face visit depending on how you are doing. The study personnel will help you find ways to take the prescribed calcium, vitamin D and exercises as instructed.
You will return for assessments at 6 and 12 months as described above.

What are the possible risks of being in this research study?
The following are potential risks you could experience during this study:

DXA and pQCT exams: DXA and pQCTs are relatively safe, non-invasive, and painless procedures. The risk associated with these tests is radiation exposure. However, the risk is small. You have already completed a whole body DXA as part of the screening process. As part of the main study you will complete a pQCT at baseline, 6 and 12 months, and additional DXAs of your whole body at 6 and 12 months.The additional exposure for the pQCT and DXA combined after enrollment in the main study is approximately 45usv and equivalent to the radiation you would receive during an airplane flight from New York City to Los Angeles. To prevent unnecessary radiation exposure, you will wear a lead apron over the majority of your body, including the breasts, during the pQCT tests.

Blood draws:There is risk of bruising and infection with any blood draw. The study personnel are all highly skilled and trained and will use strict processes to prevent bruising (pressure on the blood draw site) and the spread of germs.

Exercise
Muscle Soreness or injury: It is common to have muscle soreness after starting a new exercise program. This can often be alleviated by starting the exercise program slowly. Although injury can occur, exercises will be performed on strength training machines which help control your movements, lessening the chance of injury.

Fracture: A fracture in the bodies of the spine (vertebral compression fracture) can occur with exercise even in women with low bone mass (early stages of osteoporosis). The movement most likely to contribute to this fracture is bending and twisting with something heavy in your hand. Your exercise instruction will stress good posture and correct performance of the exercises to avoid these movements which stress the spine.

Heart problems with exercise: There is a slight risk of heart attack and even death with exercise, however, the overall risk is very low. The risk is greatest with vigorous exercise. The instructions for exercise teach you how to exercise at a moderate intensity and avoid exercise habits which raise your blood pressure and cause stress while exercising.

Calcium and Vitamin D supplementation
Vitamin D supplements are relatively safe. Too much calcium can be harmful. Stomach upset, constipation, and kidney stones have occurred with high intakes of

calcium. You are encouraged to take at least 8 glasses of water a day while you are taking calcium and vitamin D supplements. You should not take additional supplements of calcium and vitamin D supplements above those of the study protocol.

Risedronate medication to prevent bone loss

Risks associated with this medication are not common but include: 1) damage to the lining of your mouth, stomach and the tube between, possibly resulting in bleeding, 2) stomach ulcers, 3) abdominal pain, 4) esophageal cancer, 5) vomiting, 6) kidney impairment, 7) severe joint, muscle or joint pain, irregular heart rhythm. Long term use is associated with a small increase risk in unusual fractures, however, typical hip fracture rates are decreased when this medication is used properly. The most common side effect for persons taking this medicine is upset stomach. Please contact study personnel in the event of discomfort when taking this medication.
The medication is harmful to the fetus, however, this is not a factor for you since you are post-menopausal.

Questionnaires

There is minimal risk of psychological discomfort when you answer questions on the questionnaires or during interviews. You are free not to answer any of the questions on the questionnaires or you can stop the interview at any time if you feel uncomfortable.

It is possible that other rare side effects could occur which are not described in this consent form. It is also possible that you could have a side effect that has not occurred before.

What are the possible benefits to you?

Because you have low bone mass you are at higher risk for developing osteoporosis and fractures. You may be able to improve your bone health with the study treatment you receive (calcium and vitamin D supplements alone, or with risedronate or exercises).

Or, you may not get any benefit from being in this research study.

What are the possible benefits to other people?

Findings from this study may identify better ways to help women prevent bone loss and potentially prevent osteoporotic fractures during the first years after menopause.

What are the alternatives to being in this research study?

Instead of being in this research study, you can choose not to participate.
The National Osteoporosis Foundation recommends that post-menopausal women take calcium and vitamin D supplements and increase activity. It is not typical for a primary care provider to refer to a specialist with expertise in exercise programs with specific bone building capacity, however, you could seek out specialists on your own to advise on an appropriate bone building exercise program.
It is not a standard of care to test bone mineral density in all post-menopausal women. The National Osteoporosis Foundation recommends testing for women over 65 and those at high risk of osteoporosis or fracture. If you chose not to participate, you would need to discuss with your primary care provider the benefits of having a DXA test and you (or your insurance company) would be responsible for the cost.
The National Osteoporosis Foundation recommends initiation of medication to prevent bone loss such as risedronate when a woman has osteoporosis. However, in practice, many primary care providers prescribe the medication when a women has low bone mass or is osteopenic. If you chose not to be in this study, you and your primary care provider would determine if medication was indicated and when to begin medication.

What will being in this research study cost you?
There is no cost to you to be in this research study.

Will you be paid for being in this research study?
If you live less than 50 miles from Omaha, you will be paid $50 for each assessment completed: at baseline, 6 months and 12 months. If you live further than 50 miles from Omaha, you will receive $75 for each assessment completed to compensate for additional time spent traveling. If you are in the exercise group, you will be provided a 12 month YMCA or Kroc Center membership so you can access the facility to exercise for the purpose of the study. If you are in the "calcium/vitamin D only" or "risedronate" group, you will receive a 6 month YMCA or Kroc Center membership at the completion of the study if you would like. If you complete less than 6 months of the study, you will receive a 3 month membership voucher instead of a 6 month voucher.

In order to compensate you for your participation in this research study, we are required to obtain your social security number per UNMC accounting practices. If you choose not to provide your social security number you can still participate in the research study but we will not be able to compensate you for your participation.

Who is paying for this research?
This research is being paid for by grant funds from the National Institute of Health.

UNMC receives money from the National Institute of Health to conduct this study.

What should you do if you are injured or have a medical problem during this research study?
Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at the Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

UNMC has no plans to pay for any required treatment or provide other compensation. If you have insurance, your insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if your insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of your legal rights.

How will information about you be protected?
You have rights regarding the protection and privacy of your medical information collected before and during this research. This medical information is called "protected health information" (PHI). PHI used in this study may include your medical record number, address, birth date, medical history, the results of physical exams, blood tests, x-rays as well as the results of other diagnostic medical or research procedures. Only the minimum amount of PHI will be collected for this research. Your research and medical records will be maintained in a secure manner.

Who will have access to information about you?
By signing this consent form, you are allowing the research team to have access to your PHI. The research team includes the investigators listed on this consent form and other personnel involved in this specific study at the Institution.

Your PHI will be used only for the purpose(s) described in the section What is the reason for doing this research study?

You are also allowing the research team to share your PHI, as necessary, with other people or groups listed below:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB
- Federal law requires that your information may be shared with these groups:

- The HHS Office of Human Research Protections (OHRP)
- The Food and Drug Administration (FDA)
- National Institutes of Health (NIH)

- The HIPAA Privacy Rule requires the following groups to protect your PHI:
  - Researchers at Creighton University.

Your PHI may also be shared with the following groups. However, these organization(s) do not have the same obligation to protect your PHI:

- National Institutes of Health, which sponsors this research and provides funds the Institution to conduct this research
- Data and Safety Monitoring Committee (DSMC)

You are authorizing us to use and disclose your PHI for as long as the research study is being conducted.You may cancel your authorization for further collection of PHI for use in this research at any time by contacting the principal investigator in writing. However, the PHI which is included in the research data obtained to date may still be used. If you cancel this authorization, you will no longer be able to participate in this research.

How will results of the research be made available to you during and after the study is finished?

You can search this website at any time. In most cases, the results of the research can be made available to you when the study is completed, and all the results are analyzed by the investigator or the sponsor of the research. The information from this study may be published in scientific journals or presented at scientific meetings, but your identity will be kept strictly confidential.

If you want the results of the study, contact the Principal Investigator at the phone number given at the end of this form or by writing to the Principal Investigator at the following address:

Nancy Waltman, PhD, APRN-NP
UNMC, College of Nursing, Lincoln
1230 O Street
Lincoln, NE 68588-0220

Laura Bilek, PhD, PT
School of Allied Health Professions
984420 NE Medical Center
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A description of this clinical trial will be available on www.ClinicalTrials.gov, as

required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results.

What will happen if you decide not to be in this research study?
You can decide not to be in this research study. Deciding not to be in this research will not affect your medical care or your relationship with the investigator or UNMC. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

What will happen if you decide to stop participating once you start?
You can stop participating in this research (withdraw) at any time by contacting the Principal Investigator or any other research staff.

Deciding to withdraw will otherwise not affect your care or your relationship with the investigator or UNMC. You will not lose any benefits to which you are entitled.

For your safety, please talk to the research team before you stop taking any study drugs or stop other related procedures. They will advise you how to withdraw safely.

Will you be given any important information during the study?
You will be informed promptly if the research team gets any new information during this research study that may affect whether you would want to continue being in the study.

What should you do if you have any questions about the study?
You have been given a copy of "*What Do I Need to Know Before Being in a Research Study?*" If you have any questions at any time about this study, you should contact the Principal Investigator or any of the study personnel listed on this consent form or any other documents that you have been given.

What are your rights as a research participant?
You have rights as a research subject. These rights have been explained in this consent form and in The Rights of Research Subjects that you have been given. If you have any questions concerning your rights or complaints about the research, you can contact any of the following:

- The investigator or other study personnel
- Institutional Review Board (IRB)
    - Telephone: (402) 559-6463
    - Email: IRBORA@unmc.edu
    - Mail: UNMC Institutional Review Board, 987830 Nebraska Medical

Center, Omaha, NE 68198-7830

- Research Subject Advocate
  - Telephone: (402) 559-6941
  - Email: unmcrsa@unmc.edu

Documentation of informed consent

You are freely making a decision whether to be in this research study. Signing this form means that:

- You have read and understood this consent form.
- You have had the consent form explained to you.
- You have been given a copy of The Rights of Research Subjects
- You have had your questions answered.
- You have decided to be in the research study.
- If you have any questions during the study, you have been directed to talk to one of the investigators listed below on this consent form.
- You will be given a signed and dated copy of this consent form to keep.

Signature of Subject _____
Date _____

My signature certifies that all the elements of informed consent described on this consent form have been explained fully to the subject. In my judgment, the subject possesses the legal capacity to give informed consent to participate in this research and is voluntarily and knowingly giving informed consent to participate.

Signature of Person obtaining consent _____
Date _____

Authorized Study Personnel

Principal

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Secondary

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