# Enhancing Skeletal Adaptation to Exercise by Attenuating the Acute Disruption of Calcium Homeostasis During Exercise

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**Subject Name:** _____ **Date:** _____

**Title of Study:** Enhancing Skeletal Adaptation to Exercise by Attenuating the Acute Disruption of Calcium (Proof-of-Concept Study)

**Principal Investigator:** Wendy Kohrt, PhD **VAMC:** 554

**VA Investigator:** Wendy Kohrt, PhD **COMIRB#** 21-3163

You are being invited to take part in a research study that is being funded by the VA. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

**Why is this study being done?**

The goal of this study is to learn more about how exercise affects your bones. It is commonly believed that exercise increases bone density, but that does not always happen. We believe that exercise can cause your blood calcium level to decrease, and that calcium is released from bone during exercise to slow or prevent the decline in blood calcium. This study will learn more about the loss of calcium from bone during exercise.

**Other people in this study**

Up to 60 people from your area will participate in the study.

**What happens if I join this study?**

If you decide to join the study, you will participate in screening visits to the clinic to determine your eligibility. If you are eligible, you may be asked to participate in the full study.

This research study is expected to take approximately 2 years. Your individual participation in the project will take up to 10 weeks.

**Consenting Visit**

You will have the option to fast (no food or drink, other than water, for 8 hours) overnight for this visit. If you choose to fast for the consenting visit, we will do all of the procedures below in the same day. If you choose not to fast for the consenting visit, we will schedule a separate visit for the blood test, which requires that you be fasted. During this visit:

- You will have the opportunity to review and discuss this consent form and ask any questions you have and, if you are willing, to sign it.
- You will have a physical examination by a clinician and a review of your medical history.
- About 2 teaspoons of blood will be taken from a vein in your arm.

- You will also have a bone density test (DXA), which involves lying on an x-ray table for about 15 minutes. If there is any possibility that you could be pregnant, you will take a urine pregnancy test prior to your DXA.

This visit will take place at the outpatient Clinical and Translational Research Center (CTRC) on the University of Colorado Anschutz Medical Campus and will last about 1.5 hours.

**Baseline Study Visit**

**Exercise Test:** During this visit you will exercise on a treadmill for 10 to 15 minutes. It will be easy at the start and become gradually more difficult until you cannot continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal and you will breathe only through your mouth using a special mouthpiece or mask. If you have any signs of a heart problem, such as certain ECG changes, we may ask you to follow-up with a cardiologist. If further evaluation by a cardiologist shows there is no problem, you may be able to continue in the study. If you choose not to follow-up with a cardiologist, you will not be able to participate in the study.

This visit will take place at the outpatient CTRC on the University of Colorado Anschutz Medical Campus and will last about 1 hour.

**Exercise Training Visits**

If you are eligible to participate, you will come to the outpatient CTRC gym to exercise 4 days per week for 4 weeks. If you miss any sessions, the intervention will be extended so that you can complete 16 sessions. The exercise will be about 60 minutes of vigorous treadmill walking (plus a short warm-up and cool-down). You will wear a heart rate monitor so that we can adjust the speed and grade of the treadmill to keep your heart rate in the target range.

**Blood Collection Visits**

At your 1st, 8th, and 16th exercise training visits, we will collect blood before, during, and after exercise. Before each of these blood collection visits, you will be asked to record what you ate the night before you come to the clinic and you will need to fast for at least 8 hours before each of these visits (water is okay). You will bring this record with you to your visit and we will make you a copy. You will be asked to eat the same thing before the next two blood collection visits. On the day before your blood collection visits, we ask that you do only light physical activity (e.g., walking to your vehicle).

You will be asked to come to the outpatient CTRC between 7AM and 8AM for the blood collection visits. You will walk briskly on the treadmill for about 60 minutes as described above for the Exercise Training Visits

When you first get to the CTRC, we will take your heart rate and blood pressure, get your body weight in a hospital gown, ask you to empty your bladder, and then insert an IV into a vein in your arm. You will be resting when we get our first blood sample (~2 teaspoons) from the IV about 15 minutes before exercise. You will then move to the treadmill and stand for 5 minutes. A second pre-exercise blood sample (~2 teaspoons) will be taken and then you will start to exercise. During exercise, a blood sample (~2 teaspoons) will be taken from your IV every 15 minutes.

When you stop exercising, you will rest for 4 hours and we will take blood samples from your IV 15, 30, 60, 120, 180, and 240 minutes after exercise. You cannot leave the facility during this time. You will be allowed

to drink as much water as you want and we will provide a snack for you after the 120-minute blood sample. After the 240-minute blood sample, you will be allowed to leave. You will be asked to come back to the CTRC 24 hours after the end of exercise for another blood draw. You will need to be fasted for this blood draw. A total of ~26 teaspoons will be collected during exercise and recovery.

We will also collect urine immediately after exercise and 240 minutes after exercise. You will be asked to provide another urine sample at your 24-hour visit.

These steps will be repeated at the next two blood collection visits.

**What are the possible discomforts or risks?**

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur.

Discomforts you may experience and possible risks of the study include:

- **Exercise**: The potential serious risks of exercise testing and training include irregular heartbeats, heart attack, cardiac arrest, and death, but these are very rare. Less serious risks include injury to joints or muscles and feeling lightheaded or dizzy. Exercise can also lead to dehydration. There is a minor risk of skin irritation from the electrodes we use to track your heart rate. These risks are minimized by a review of your medical history and physical exam before the exercise test, and by monitoring your heart and blood pressure before, during, and after exercise testing. If your heart or blood pressure responses are not normal, we may not perform the test, stop the test early, or complete the test but not enroll you in the study.
- **Fasting**: You will be asked to fast prior to your screening blood draw and before each of your blood collection visits. As a result of fasting, you may feel faint, lightheaded, or could pass out. If you are not feeling well, we may not perform the test or stop the test early.
- **Blood Draws**: For visit 1 we will take about 2 teaspoons of blood from your vein. For each of the three blood collection visits (exercise training visits 1, 8, and 16), we will take about 26 teaspoons of blood from your vein. We will get blood samples by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin. You may feel faint during the blood draw. When we have to get multiple blood samples on exercise training visits 1, 8, and 16, we will insert a needle with a small plastic tube into one of your veins. The needle is removed but the plastic tube, or catheter, stays in place, which allows us to get multiple blood samples without using a needle each time. You will have the catheter in your arm about 5.5 hours. The IV catheter can cause an infection or blood clot, but this is very rare. You may have some redness, swelling, or bruising at the IV site.
- **DXA**: During visit 1 we will perform 2 sets of DXA scans of your whole body, spine, and hip (6 scans total) to measure your bone density. The second set of scans will be performed immediately after the first scan. You will lie still for a few minutes for each scan while an X-ray takes a picture. X-rays are a type of radiation. These scans will give you about the same amount of radiation you get from your environment (for example, from the sun) in 4 days.
- **Confidentiality and Privacy**: There is a risk that people outside of the research team will see your research information. We will do all that we can to protect the privacy of your information, but it cannot be guaranteed.
- **Unknown Risks:** The study may include risks that are unknown at this time.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

**What are the possible benefits of the study?**

This study is designed for the researcher to learn more about exercise and bone health.

This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the Discomforts or Risks.

**Who is paying for this study?**

This research is being sponsored for by the VA Clinical Science Research and Development Service.

**Will I be paid for being in the study?**

You will be paid $100 for each of your blood collection visits for a total of $300 for all 3 visits. If you leave the study early, or if we have to take you out of the study, you will only be compensated for the visits you completed.

It is important to know that payments for participation in a study are taxable income.

The VA will be disbursing your payments. Your SSN will be collected and used to report this taxable income to the IRS.

The payment will be made via a payment voucher.

**Will I have to pay for anything?**

You will be responsible for your transportation costs to and from the research facility. Otherwise, there will be no cost to you for participation in this study. However, some Veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by the VA that are not part of this study. If you decide to participate in this study, you cannot be charged nor your insurance billed, for research-related interventions or procedures that are required by the protocol.

**Is my participation voluntary?**

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If there are any new findings during the study that may affect whether you want to continue to take part, you will be told about them.

**Can I be removed from this study?**

The study doctor may decide to stop your participation without your permission, if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

**What happens if I am injured or hurt during the study?**

Every reasonable safety measure will be used to protect your well-being. The VA Eastern Colorado Health Care System (ECHCS) will provide necessary medical care and treatment for any injury that is a result of participation in this study for veterans, in accordance with applicable federal regulations (38 CFR 17.85). Compensation for such an injury may be permitted by applicable federal laws and/or regulations. The VA is not required to provide treatment for injuries in research studies if the injuries are caused by your non-compliance with study procedures.

You should inform your care provider(s) if you decide to participate in this research study. If you have questions about an injury related to the research, call [redacted] between 8AM and 5PM.

If you have an injury while you are in this study, you should call [redacted] Emergency and ongoing medical treatment will be provided as needed.

**Who do I call if I have questions?**

The researcher carrying out this study at the VA is Wendy Kohrt, PhD. You may ask any questions you have now. If you have any questions, concerns, or complaints later you may call [redacted]. You will be given a copy of this form to keep.

If you have questions regarding your rights as a research subject, concerns or complaints about this research study, please call the Colorado Multiple Institutional Review Board (COMIRB) office at [redacted]. This is the Board that is responsible for overseeing the safety of human participants in this study. If you want to verify that this study is approved or if you would like to obtain information or offer input, please contact the VA Research Office at [redacted]

**How will my private information be protected?**

Taking part in this study will involve collecting private information about you. We will keep all research records that contain your identifiable health information, confidential to the extent allowed by law. Records about you will be kept in locked filing cabinets in a locked office or on password-protected computers accessible by study personnel.

We will try to keep your medical records confidential, but it cannot be guaranteed. Records that identify you (including your medical records and the consent form signed by you), may be looked at or portions of your records copied that identify you by others.

There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the VA Institutional Review Board (IRB), our local Research and Development Committee, and other study monitors may look at or copy portions of records that identify you. (If the study involves a product regulated by the FDA, the Food and Drug Administration should be included in the above list)

The data and blood and collected from you are important to this study and to future research. Future tests will not include any DNA, RNA, or genetic analysis. If there is any unused blood left at the end of this study, we will

store it for potential future measurements related to the biology of aging tissues in response to exercise. Only the investigators involved in this study will be allowed to use these samples for research, which may include some experiments not directly related to the study you are participating in. Samples will be stored using a unique code that cannot be used to personally identify you until they are used up or no longer of good quality. There are no known commercial benefits related to your banked samples.

We will include information about your study participation in your medical record.

A description of this clinical trial will be available on http://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. You can search this website at any time.

Identifiers might be removed from the identifiable private information, data, or identifiable biospecimens that are collected. After that removal, the 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.

**Who will see my research information?**

We will try to keep your medical records confidential, but it cannot be guaranteed. Records that identify you (including your medical records and the consent form signed by you), may be looked at or portions of your records copied that identify you by others. These include:

- Federal agencies such as the Food and Drug Administration (FDA), the General Accountability Office (GAO), the Office of the Inspector General, Office for Human Research Protections (OHRP), and the Office of Research Oversight (ORO) that protect research subjects like you, may also copy portions of records about you.
- People at the Colorado Multiple Institution Review Board
- The investigator and research team for this study
- The sponsor (VA Clinical Science Research and Development group paying for the study), study monitors or agents for the sponsor
- Officials at the institution where the research is being conducted, and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research
- Our local VA Research and Development Committee
- UC Denver and its Clinical Trials Management System

I understand that by signing this consent form, a copy of limited data about me, restricted to (list data elements or state “all research data”) that is collected as part of this specific VA research study will be stored in the REDCap database (or Data Storage System) that is supported by the national VA or by the University of Colorado Denver’s (UCD’s) Colorado Clinical and Translational Sciences Institute (CCTSI). This data will be used solely for the purposes defined in this consent form and for this specific study. Data collected about me for this study placed on the VA or CCTSI REDCap Database will not be accessed or used for any other study

or purposes, and will only be accessed by VA-credentialed personnel. The CCTSI REDCap Database is a highly secure, nationally-utilized data management system, and it is housed within the highly-secure environment at the University of Colorado Denver.

Information about you will be combined with information from other people taking part in the study. We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

We will ask you to sign a different form that talks about who can see your research records. That

form is called a HIPAA Authorization form. It will mention companies and universities who will se

your research records.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study has been completed.

The HIPAA Authorization form that you will also be asked to sign will state when or if it expires. However, you may withdraw this authorization for use and disclosure of your personal health information by providing written request to the Investigator. If you withdraw the HIPAA Authorization form, the Institution, the Investigator, the research staff, and the research Sponsor will no longer be able to use or disclose your personal health information from this study, except so far as that they have already relied on this information to conduct the study.

**Agreement to be in this study**

I have read this form. A member of the research team has explained the study to me. I have been told about the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

By signing this form below, I voluntarily consent to participate in this study. I will receive a copy of this consent after I sign it. A copy of this consent form will be placed in my medical record.

Participant's Signature: _____ Date:_____

Print name: _____

Consent form explained by: _____ Date: _____

Print name: _____

**OPTIONAL ADDITIONAL PROCEDURES**
**Optional Consent for Data and Specimen Banking for Future Research**

The researchers affiliated with the VA Eastern Colorado Geriatric Research, Education, and Clinical Center (GRECC) would like to keep some of the blood and serum that is taken during the study but is not used for other tests. [redacted] is a member of this research group, which includes researchers and staff at the VA Eastern Colorado Healthcare System and many are affiliated with the University of Colorado Anschutz Medical Campus. If you agree, the blood and serum will be kept and may be used in future research to learn more about how bone responds to exercise. The research that is done with your blood and serum samples is not designed to specifically help you. It might help people who have osteoporosis and other diseases in the future. Reports about research done with your blood and serum samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your blood and serum samples will not affect your care.

The choice to let the VA Eastern Colorado GRECC keep the blood and serum samples for future research is up to you. No matter what you decide to do, it will not affect the care you receive as part of the study. If you decide now that your blood and serum samples can be kept for research, you can change your mind at any time and contact [redacted] to let her know you do not want the research group to use your blood and serum samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until the VA Eastern Colorado GRECC decides to destroy them, but no longer than 10 years.

When your blood and serum samples are given to other researchers in the future, [redacted] will not give them your name, address, phone number or any other information that will let the researchers know who you are. Sometimes blood and serum samples are used for genetic research (about diseases that are passed on in families). Even if your blood and serum samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your blood and serum samples will only be used for research and will not be sold. The research done with your blood and serum samples may help to develop new products in the future, but there is no plan for you to be paid.

Sometimes data and samples are used for genetic research (about diseases that are passed on in families). Even if your data and samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

We may share data from our research with other researchers or data banks. One such data bank is called dbGAP, which collects genetic and other data and is sponsored by the National Institutes of Health. By broadly sharing data in data banks like this, we can make our discoveries more accessible to other researchers. Information which directly identifies you will not be sent to these data banks.

Because your genetic information is unique to you, there is a small risk that someone could connect the information back to you. Also, genetic research and broadly sharing data may involve risks to you or people like yourself that are unknown at this time.

The possible benefits of research from your blood and serum samples include learning more about what causes osteoporosis and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. The VA Eastern Colorado GRECC will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by the research group.

Please read each sentence below and think about your choice. After reading each sentence, check "yes" or "no" and initial. If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.I give my permission for my data and blood to be stored in a central tissue bank at the VA Eastern Colorado GRECC or the Rocky Mountain Regional VA for future use by the study investigators:

1. I give my permissions for my data and blood samples to be kept by the research team for use in future research to learn more about how to prevent, detect, or treat diseases or conditions related to aging.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my data and blood samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   ☐ Yes ☐ No _____Initials

3. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials

**Re-contact.** If you wish to re-contact the subject for future research, specify whether the subject will be contacted from within the VA **or** outside of the VA **and use the following**:

☐ Yes, I am interested in being contacted to participate in future studies. ____Initials

☐ No, I am not interested in being contacted to participate in future studies. ____Initials