

Official Title:

Relationship of Exercise, Sleep, and Inflammation Markers in People Living With HIV

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Study Title: The HEALTH Study

Key Information:

Please read all the information below and ask questions about anything you don't understand before deciding if you want to take part.

You are being asked to be in a research study. Participation in research is voluntary.

Purpose of this study: The purpose of this study is to learn more about what types of exercise has the best results with regards to improvement in muscle function and decrease in fatigue and what helps people aging with HIV continue to exercise on their own.

Procedures: If you agree to participate, the following will happen:

- There are 3 visits in the Screening phase to see if you are eligible for the study. If you qualify and want to continue to participate, you will be randomly assigned to 1 of 2 different types of exercise (Continuous Moderate Intensity or High Intensity Interval training). You do not get to choose which arm of the study you are in.
- Participation in the exercise phase involves exercising in either our exercise center or a recreational center 3-4 days/week for about 4 months (16 weeks) and then an additional 3 months of exercising on your own. Total participation in the study could be up to 9 months.
- If you agree to participate, you will be asked to be in optional parts of the study, including an extra follow up visit at the end (12 month follow up).

Risks: Participation in this study involves risks, including the following:

- Muscle and joint pain, alteration in heart rate, changes in blood pressure, healthcare exposures (risk of exposure to infection) due to exercising around others, exposure to radiation, pain/bruising from blood draws/muscle biopsies, being tired or bored during tests of thinking abilities, dizziness/lightheaded from exercise/blood draws/fasting, claustrophobia from MRI.

Benefits: There is no guarantee that your health will improve if you join this study. This study may lead to information that could help patients and health care providers in the future.

Detailed Consent:

Why is this study being done?

This study plans to learn more about how exercise changes muscle strength and muscle function in people aging with HIV.

Exercise has many beneficial effects, including an improvement of muscle function with aging. We don't know the best kind of exercise for people with HIV. We also don't know how we can best help people continue exercising long term. The purpose of this study is to:

1. Test which type of exercise leads to the biggest improvement in muscle function and reduction in fatigue.
2. See what helps people keep exercising on their own, after exercising in a gym with a trainer.

3. Optional sleep sub-study- Test which type of exercise leads to the biggest improvement in sleep quality.

You are being asked to be in this research study because you are aging with HIV and are not currently exercising regularly.

Other people in this study

Up to 100 people from your area will participate in the study.

Up to 300 people around the country will be in the study.

Sleep sub-study approximately 15 people from your area.

What happens if I join this study?

If you join the study, the following will happen:

Initial screening visit

- At the initial screening visit, you will answer several questions about your medical problems and medications you take. You will complete a few surveys.
- You will have your blood pressure, height, and weight measured.
- Then you will have an exercise test to find out if your heart is healthy. This will involve walking or running on a treadmill for about 10 minutes. You will breathe through a special mouthpiece during this test. The exercise will be easy at first, but will gradually become more difficult until you can no longer continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal.

Screening visit 2,3, and 4

- You will have a blood draw
 - *There is a possibility that blood work may need to be repeated or redrawn at a subsequent screening visit if there is a problem with the sample.
- We will measure your muscle function through several tests and measure body composition using DXA scan
- A urine pregnancy test will be administered prior to a DXA scan for women who are currently still menstruating
- You will also have the option of completing a muscle biopsy, MRI/MRS scan, and a muscle ultrasound.
- You will also have the option of completing some tests and surveys on your thinking and daily abilities.
- *If you meet the requirements* and want to continue to take part in the study, you will:
 - 1) Be assigned randomly (a process similar to flipping a coin) to 1 of 2 different types of exercise: continuous moderate intensity or high intensity interval training. You do not get to choose which arm of the study you are in.
 - 2) Exercise regularly in our exercise center or a similar exercise facility 3 to 4 days per week for about 4 months (16 weeks). The facility will need to meet certain criteria and will need to be approved by the research team.
 - 3) Be assigned randomly to 1 of 2 different types of follow-up: more intensive or less intensive text messaging.
 - 4) Complete an additional 3 months of exercise on your own.
 - 5) Be asked to be in optional parts of the study
 - 6) Have the option to participate in interviews to tell us how exercise is going and your thoughts about exercise.
 - 7) Have several visits to test your muscle function and complete surveys throughout the study.

- 8) Have a post-exercise research visit. This visit will include the option to complete a 2nd muscle biopsy.
- 9) Complete a visit after the study is over to check-in (12 months after starting exercise).

The above procedures will take about 7 months. With the time for screening and completing study visits, the total time that you are involved with the study may be up to 9 months. If you choose to do the additional follow-up, your time in the study may be up to 14 months.

Here, we will describe in more detail what the study will involve. Please be sure to ask questions if you have any:

- 1) **Exercise program-** The goal of the exercise program is to build muscle mass and improve your ability to exercise over 4 months. You will come to our exercise center or a similar facility 3 to 4 days a week. Each session will take about 1 ½ hours.

You will do a variety of exercises that build muscle mass, such as walking, jogging, and weight lifting. You will start at a lower intensity while you learn the exercise, but the goal will be to gradually increase to a more moderate or intense exercise. For each exercise session, you will have a list of exercises for the day. You will write down information on what you complete (exercise log).

You will continue to exercise after the first 4 months at a place that you chose. This could be at your home, outside, or at a gym.
- 2) **Research Tests—** The research tests are shown on the table below. Most of the research tests will be completed at a Pre-Exercise and a Post-Exercise Visit. These visits will last up to 3 hours (if you chose to have a muscle biopsy), or about 2 ½ hours if you do not have a muscle biopsy. All of the tests are done for research purposes and all are voluntary.
 - **Exercise capacity-** This will involve walking or running on a treadmill for about 10 minutes. You will breathe through a special mouthpiece during this test. The exercise will be easy at first, but will gradually become more difficult until you can no longer continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal. In addition to the screening visit, you will also have this after about 4 months (week 16).
 - **Muscle biopsy (optional)–** This test involves taking a small piece of leg muscle so that we can try to learn how exercise changes the muscle. You will be asked to abstain from alcohol or caffeinated beverages (coffee, cola, etc) after 1:00 p.m. the day prior, and to fast from any food or drink beginning at 9 p.m. with the exception of water and medications. You will arrive the following morning for the biopsy. After getting numbing medicine (lidocaine), a small cut (about one-quarter of an inch) is made in your thigh and a small piece of muscle is removed. This takes about 60 minutes.
 - **MRI/MRS (optional)—**This involves lying flat in the MRI machine for about 15 minutes. You will be asked to avoid vigorous activity for 2 days prior to the scan. You will be asked to push your foot against a pedal for 90 seconds and then to relax for 8 minutes. The MRI will scan your left thigh and calf.
 - **Muscle ultrasound (optional)—**This involves lying flat on a treatment table for a maximum of 30 minutes. We will apply moderate pressure with an imaging probe over several upper and lower body muscles to take images of your muscle structure.
 - **Stool Collection (optional)-** This involves collecting a small sample of your stool (poop). We will provide you with a device you can place under the toilet seat to collect the stool. You will use a wooden stick to transfer some of your stool to a collection cup. The sample cup will be stored in your freezer in paper bag until you come for your next research visit. The device to collect the stool and the stick are thrown into the trash.
 - **Blood tests –** We will draw between 2 and 5 tablespoons of blood at up to 4 of the visits. These visits will be in the morning after an overnight fast (nothing to eat or drink except water, for 8 hours).
 - **Activity monitor –** For 1 week at the beginning, the middle, and monthly during Part 2 of the study, you will wear a small monitor that records your activity. You will need to bring the monitor and log with you to your next visit.
 - **DXA scan –** This test will measure your muscle, fat, and bone. The test involves lying still on a table for about 30 minutes.

- **Interviews (optional)** —At up to 4 visits, if you agree to participate, one of our research team members will have a one-on-one discussion with you about your thoughts on the study, on your ability to keep exercising, and about how you feel with exercise. If you decide to decline participation before starting exercise or withdraw from the study, a decline/withdrawal interview may be offered to you to determine your reasons behind your decision and/or ways to improve the study intervention. This meeting will be held in a private setting (an exam room, phone, or by secure zoom), and will be audio-recorded. Your name and identifying information will not be recorded.
- **Physical function** – These tests will include 1) the time to rise from a chair 10 times without using your hands, 2) the time it takes you to walk 400 meters (about 400 yards), 3) the time it takes you to walk 4 meters, and 4) a balance test, and 5) grip strength. These tests will take about 20-30 minutes for all of the testing, which will be measured at baseline, week 16, and the end of the study. Two of the tests will be measured once a month (will occur at the research center).
- **Muscle strength** - For this test you will start with light weights and gradually try to lift heavier weights until you feel that you have lifted as much weight as you can using proper lifting form. This test takes about 1 hour. You will do this in place of one of your regular exercise training visits (will occur at the research center).
- **Surveys**—Throughout the study, you will complete several paper surveys on your fatigue, activity, and sleep. The time to complete these surveys will be about 20-30 minutes. In addition, you will record what you eat for 3 days at the beginning of the study and again after part 1 (after about 4 months of exercise). At the 12-month visit you will complete some surveys through text messaging. We will send a text message to your phone with a link to complete a survey in the morning and in the evening for 7 days.
- **Health Status**- Once per month while you are exercising, we will ask you to complete a form regarding any changes in your medical history. Although you will notify us using this form, *please be sure to let us know right away when you have had any changes in your medications, visits to the doctor, or any other changes.*
- **Tests on thinking abilities (optional)** — at up to 4 visits, we will ask you to complete some tests that measure how quickly you think, your ability to solve problems, and your memory. For some of these tests your responses will be audio-recorded. Your name and identifying information will not be recorded. This should take about 1 hour.

						Part 1 Week Number							Part 2 Week Number				12 month follow-up (optional)
Test	Screen #1	Screen #2	Screen #3	Screen #4	0	2	4	8	12	16	End Part 1	4	8	12	End Part 2	48*	
Exercise capacity	X									X							
MRI/MRS*				X							X						
Muscle biopsy*		X									X						
Muscle ultrasound*			X							X							
Blood draw		X								X						X	
Wear activity monitor		X									X	X	X	X		X	
Collect stool sample*		X									X						
Microbiome Questionnaire		X									X						

(Collected with stool)*																
Urine Pregnancy test (if menstruating)			X								X					
DXA scan			X								X					
Interviews*			X								X				X	
Physical function**			X		X		X	X	X	X	X	X	X	X	X	
Muscle strength**						X	X	X	X	X	X				X	
Fatigue questions**			X		X		X	X	X	X	X	X	X	X	X	
Other surveys			X								X				X	X
Health status					X		X	X	X	X		X	X	X	X	
Thinking ability tests*		X									X				X	X

*optional test; optional visit done 12 months after starting the intervention (part 1 of study).

** Muscle strength, physical function, and fatigue questions will be assessed every 2-4 weeks. These will occur either just before/after or during a regular exercise session and will not require an additional visit.

Optional Sleep sub-study- Screening Visit #1: Consent, medical history and sleep survey administration.

Consent: After obtaining informed consent, the first of two baseline visits will include medical history, Respiromics actiwatch initiation, provide sleep diary and sleep survey administration (Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance). Please note, the medical history, PSQI and PROMIS SF are already collected as part of the ongoing HEALTH study.

Actiwatch Initiation and Sleep Diary: The RA will initialize the participant's actiwatch and instruct each participant on proper use of the actiwatch (Phillips Respironics Actiwatch Spectrum Plus). During initialization the RA will enter all required demographic information. If a participant is transgender, sex assigned at birth should be used, as the variable of sex does not impact the data. Participants will be asked to wear the device for 10 consecutive days at baseline and again post 16-week intervention. The actiwatch, which resembles a wristwatch and is worn on the non-dominant wrist. The device should be fully charged. While wearing the actiwatch, participants will be instructed to complete a corresponding **10-day sleep diary** that will collect information including time each participant went to bed, wake time, time out of bed, how many times they awoke during the night, and naps taken during the day. This information will be used to score the actiwatch data to determine our primary outcome, sleep quality. Collected data will include weekday and weekend days in the 10-day period of time. Participants should be instructed to wear the actiwatch for 10 days, 24 hours per day, except when bathing or swimming.

Sleep Surveys: Sleep quality and patterns of sleep will be evaluated using the validated Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance. The PSQI measures seven domains of sleep: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. The PROMIS Short Form –Sleep Disturbance measures sleep disturbance during the past week.

Screening Visit #2 (approximately 8 days' post baseline visit 1): Fasting blood draw after refraining from exercise for ≥ 48 hours, return actiwatch and sleep diary, and sleep survey administration.

Blood Draw: A fasting blood draw will be taken at the beginning of the second baseline visit, collected between 6:30 – 10:00 am. The participant should refrain from exercise for ≥ 48 hours. The clinical blood draw should include:

- 10 ml K2EDTA tube (plasma will be collected for analysis for inflammatory markers)

The primary inflammation markers of interest are IL-6, IL-10, IL-13, IFN- γ , CRP and TNF- α due to prior association with sleep quality, other inflammation markers, IL-1 β , IL-2, IL-4, IL-8 and IL-12p70 will be exploratory to identify potential pathways of sleep impairments.

Sleep Surveys: The Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance forms should be completed to measure sleep quality and patterns of sleep.

Return of actiwatch and sleep diary (approximately 10 days after screening visit #2): The RA will collect the actiwatch and sleep diary from the participant. The RA will check wear time for the actiwatch. If the participant did not meet wear time criteria (wearing the device for ten days), the RA will ask the participant if they are willing to wear the device again for approximately ten days. If they are willing to re-wear the device, the participant should be reinstructed on proper use and wear time criteria and provide the participant with a new sleep diary. The RA should also check the sleep diary for completeness. If the participant did not complete or has missing data in the diary the RA should assist the participant with completion of any missing data, if possible.

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Intervention Week 8 Visit (midpoint of intervention): Fasting blood draw after refraining from exercise for $\geq$ 48 hours and sleep surveys. The procedures are described above.

Intervention Week 16 Visit (completion of intervention): Fasting blood draw after refraining from exercise for $\geq$ 48 hours, actiwatch initiation, sleep diary and sleep survey administration. The procedures are described above.

End of Study Visit: Return actiwatch and sleep diary. The procedures are described above.

Sleep sub-study tests	Screening visit #1	Screening visit #2	10 days post screening visit #2	Intervention Week 8 visit	Intervention Week 16 visit	End of study
Actiwatch initiation		X			X	
Actiwatch return		X	X			X
Sleep diary initiation		X			X	
Sleep diary return		X	X			X
Sleep surveys	X	X		X	X	
Blood draw		X		X	X	

What are the possible discomforts or risks?

- **Exercise testing, exercise training, strength tests, physical function tests** — When you exercise, there is a chance that you will feel pain in your muscles or joints, feel dizzy or faint, have irregular heartbeats, have low or high blood pressure, have a slow or fast heart rate, have a stroke or heart attack, or die. The risk of death from an exercise test has been estimated to be 1 in 100,000. The risk of a heart attack is about 4 in 10,000 and the risk of a problem that would require hospitalization (for example, chest pain) is about 2 in 1,000.
- **Healthcare exposures** - Your research visits and exercise sessions will be conducted in a building with other staff and study participants. We will take all precautions to minimize your risk for exposure to any infections, including but not limited to COVID-19. To limit exposures, you should wear a mask when coming into the research center, wash your hands with soap and water regularly, and avoid coming to visits if you have any symptoms of an infection such as COVID-19, including fever, cold symptoms, loss of taste or smell, shortness of breath. You should also call your study team and stay home if you have a known or possible exposure to someone with COVID-19. This risk may be higher at other facilities.
- **DXA scans** – As part of this study we will perform DXA scans of your total body. A DXA is a way of looking inside your body using X-rays. X-rays are a type of radiation. Everyone gets some radiation from their environment every day. The total radiation dose you will receive from the DXA is less than the amount of radiation that you would receive from your environment 1 day. This radiation dose involves minimal risk and

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is necessary to obtain the research information desired.

- **Blood tests** – Throughout the study, we will need to get a total of up to 17 tablespoons of blood from you over 9 months. If we need to repeat some of the blood tests, this may increase to about 20 tablespoons. We will get blood by putting a needle into your veins and letting the blood flow into a plastic 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 your skin.
- **Fasting**—You will be asked to avoid drinking anything other than water and avoiding eating anything after midnight until blood draw or muscle biopsies are completed on some of the visits. Fasting, or not eating for a period of time, can sometimes make you feel tired, dizzy, lightheaded, or even nauseous. Drinking plenty of water, ensuring you have a regular meal the evening before, and holding diabetes medicines until you have eaten (if diabetic) can help to minimize these symptoms.
- **Muscle biopsy (optional)** – In this study we will need to take 2 small samples of your leg muscle. This procedure is called a “biopsy”. Before we take the samples, we will give you some medication to numb the area. We will then make a small cut in the skin and take the samples by pressing a hollow needle into your muscle. When we take the needle out, it will remove a small circle of muscle called a “plug”. There are some risks to taking a sample of muscle this way. During the biopsy you may feel some pain. Tenderness and bruising at the tissue sampling site is common, and this can sometimes last several days. There is a small chance that you could get an infection where the needles goes in. There is also a small chance that you could have an allergic reaction to the numbing medicine. After your skin heals up, you will have a small scar where we take the sample.
- **MRI and MRS (optional)** -- You may develop claustrophobia in the magnet or a mild muscle cramping during the exercise portion of the scan. You will not be able to perform the scan if you have any implanted devices (i.e. pacemaker or insulin pumps) The MRI machine may also be loud, you will be provided with ear plugs to help increase comfort.
- **Muscle Ultrasound (optional)** – For this test, we will run a probe that will take ultrasound images of your muscles. If you have sore muscles, you may experience slight pressure from the probe. We will use a small amount of gel on your skin over the area that we probe, which may leave a small amount of residue. We will wipe off excess gel after the images have been taken.
- **Stool sample (optional)** - You might feel uncomfortable or embarrassed collecting your stool sample. You will be provided with gloves and all of the needed equipment to minimize any contact with the sample. We encourage you to wash your hands thoroughly after collecting the sample.
- **Activity monitor**- This is a small device that you will wear continuously during the day. This can be bothersome to make sure that you always have your monitor with you.
- **Surveys**—You may feel embarrassed or uncomfortable when answering some of the survey questions.
- **Tests of thinking abilities** -- You may feel tired or frustrated during the tests of thinking abilities. No one does well on all the tests. You can stop at any time.
- **Confidentiality and privacy**: You may feel embarrassed when answering any of the questions for this study. We will do all that we can to protect your information. Any information that you share with the researcher involving use of illegal substances (such as cocaine or other drugs) will be protected. But there are some things we cannot keep private. If you give us information about hurting yourself, we will refer you immediately to a provider in the clinic or the Emergency Department. If you give us information about someone hurting someone else, we have to report that to the police. If you have a new diagnosis of HIV during the study, we will have to notify the health department. Finding out you have HIV may make it hard for you to get insurance. If a court orders us to hand over your study records, we have to hand them over to the court. There is a risk that people outside of the research team will see your research information.
- This study has been issued a Certificate of Confidentiality from the federal government to help protect your

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privacy. The Certificate prohibits the researchers from disclosing your name, or any identifiable information or document from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings. These protections apply only to your research records. The protections do not apply to your medical records. The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:

- To those connected with the research,
 - If required by Federal, State or local laws,
 - If necessary for your medical treatment, with your consent,
 - For other scientific research conducted in compliance with Federal regulations,
 - To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or
 - Under other circumstances with your consent.
- The study may include risks that are unknown at this time.

What are the possible discomforts or risks in the optional sleep sub-study?

- *Blood tests* – We will collect 10 milliliters or approximately 2 teaspoons of blood from you. We will get blood by putting a needle into your veins and letting the blood flow into a plastic 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 your skin.
- *Fasting*—You will be asked to avoid drinking anything other than water and avoiding eating anything after midnight until the blood draw is completed on some of the visits. Fasting, or not eating for a period of time, can sometimes make you feel tired, dizzy, lightheaded, or even nauseous. Drinking plenty of water, ensuring you have a regular meal the evening before, and holding diabetes medicines until you have eaten (if diabetic) can help to minimize these symptoms.
- *Actiwatch*—This is a small device that you will wear continuously during the day and at night. This can be bothersome to make sure that you always have your monitor with you.
- *Surveys*—You may feel embarrassed or uncomfortable when answering some of the survey questions.
- *Confidentiality and privacy*: You may feel embarrassed when answering any of the questions for this study. We will do all that we can to protect your information. But there are some things we cannot keep private. If you give us information about hurting yourself, we will refer you immediately to a provider in the clinic or the Emergency Department. If you give us information about someone hurting someone else, we have to report that to the police. If you have a new diagnosis of HIV during the study, we will have to notify the health department. Finding out you have HIV may make it hard for you to get insurance. If a court orders us to hand over your study records, we have to hand them over to the court. There is a risk that people outside of the research team will see your research information.
- The study may include risks that are unknown at this time.

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What are the possible benefits of the study?

This study is designed for the research team to learn more about the type of exercise that leads to the most improvement in muscle in people with HIV. The study will also help the research team know the best ways to help people keep exercising. The Sleep sub-study is designed to learn more about the type of exercise that leads to improved sleep quality in people with HIV.

This study is not designed to treat any illness and there is no guarantee that your health will improve if you join this study. 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 by the National Institutes of Health.

Will I be paid for being in the study?

- You will be compensated for your participation in this study. The payments will be combined and provided by a check 1) after the screening is completed, 2) after week 16 (End of part 1), 3) at the end of the main study (End of part 2), and 4) if you complete the optional visit 12 month visit.
- You will be paid \$50 if you complete the entire first screening visit.
- You will be paid \$35 for the second screening visit (*including wearing and returning the activity monitor*).
- You will be paid \$35 for the third screening visit.
- You will be paid \$75 each time if you complete the optional thinking tests (up to 3 times during the main study visits).
- You will be paid \$75 for each MRI/MRS visit (one at beginning and one at the end of the study).
- You will be paid \$150 for each muscle biopsy visit (one at the beginning and one at the end of the study).
- You will be paid \$20 for each muscle ultrasound assessment (one at the beginning and one at the end of the study).
- You will receive \$25 for each of the in-person physical function and fatigue checks during the second part of the study (3 total).
- You will receive \$50 for completing the week 16 visit (*including wearing and returning the activity monitor*).
- You will receive \$50 for the final main study visit (*including wearing and returning the activity monitor*).
- You will receive \$125 for completing an optional visit approximately 12 months after you start exercise (*including wearing and returning the activity monitor, and responding to most of the text message surveys*).

This will add up to a total of \$1135 if you complete all of the visits including muscle biopsies, MRI/MRS scans, muscle ultrasounds, tests of your thinking abilities, and the 12 month follow up. This will add up to a total of \$295 if you complete all the visits, but do not have the muscle biopsies, MRI/MRS scans, muscle ultrasounds, tests of your thinking abilities, and the 12 month follow up.

If you decide to complete the intervention at an approved exercise center, fees will be paid directly to the facility.

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If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed. It is important to know that payment for participation in a study is taxable income.

Sleep Sub-study-

- You will be paid \$20 for the first screening visit
- You will be paid \$35 for the second screening visit, \$20 for completion of the fasting blood draw and sleep surveys and \$15 for return of the completed Actiwatch and sleep dairy.
- You will be paid \$20 for the completion of blood draw and sleep surveys at the intervention week 8 visit.
- You will be paid \$20 for the final end of study visit (including wearing and returning the Actiwatch)

Will I have to pay for anything?

It will not cost you anything to be in the study, other than the costs of traveling to and from our facility. However, if one of the medical tests (for example, the treadmill exercise test) reveals a potential health problem that requires further evaluation, you will need to be cleared by your own health care provider if you want to take part in the study. *This may lead to added costs to you or your insurance company. You are encouraged to ask questions about these possible costs.*

In the second half of the study, we ask that you continue exercising. We may also provide you with some tools such as educational materials and an activity monitor to help you do this.

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 you leave this study, you will still receive your normal medical care. 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?

If you have an injury while you are in this study, you should call Dr. Erlandson immediately. Her phone number is 303-724-4941 during normal business hours. If an injury occurs after normal hours, please call the hospital operator at 720-848-0000 and ask to have Dr. Erlandson paged. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Dr. Kristine Erlandson. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Erlandson at 303-724-4941. You will be given a copy of this form to keep.

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You may have questions about your rights as someone in this study. You can call Dr. Erlandson with questions. You can also call the Institutional Review Board (COMIRB). You can call them at 303-724-1055. 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.

Optional Components of the Study (Muscle biopsy, stool collection, interviews, sleep sub-study)

If you decline to participate in these portions of this study, you cannot take part in these optional procedures, but you can still participate in the main study. Please state if you agree or not to the optional procedures and insert your initials.

1. Do you agree to participate in the **muscle biopsy** portion of the study?

☐ Yes ☐ No _____Initials

2. Do you agree to participate in the **stool collection** portion of the study?

☐ Yes ☐ No _____Initials

3. Do you agree to participate in the **interview** portion of the study?

☐ Yes ☐ No _____Initials

4. Do you agree to participate in the sleep study portion of the study?

☐ Yes ☐ No _____Initials

5. Do you agree to participate in the **MRI/MRS** portion of the study?

☐ Yes ☐ No _____Initials

6. Do you agree to participate in the **muscle ultrasound** portion of the study?

☐ Yes ☐ No _____Initials

7. Do you agree to participate in the **tests of your thinking abilities**?

☐ Yes ☐ No _____Initials

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8. Do you agree to participate in the **12 month follow up** portion of the study?

☐ Yes ☐ No _____Initials

Optional Consent and Authorization for Data and Specimen Banking for Future Research

Dr. Erlandson would like to keep some of the data, blood and tissue that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about muscle, aging, and exercise in people with HIV. The research that is done with your data and samples is not designed to specifically help you. It might help people who have HIV and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Erlandson keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want her to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Erlandson decides to destroy them.

When your data and samples are given to other researchers in the future, Dr. Erlandson will not give them your name, address, phone number or any other information that will let the researchers know who you are.

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 data and samples include learning more about what causes muscle weakness with aging and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. Erlandson 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 Dr. Erlandson.

Consent and Authorization Form

Please read each sentence below and think about your choice. After reading each sentence, circle “yes” or “no.” 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, blood and tissue to be stored in a central tissue bank at The University of Colorado for future use by the study investigators:

1. I give my permissions for my data, blood and tissue samples to be kept by Dr. Erlandson for use in future research to learn more about how to prevent, detect, or treat muscle weakness with aging.

☐ Yes ☐ No _____ Initials

2. I give my permissions for my data, blood and tissue 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

Who will see my research information?

The University of Colorado Denver | Anschutz Medical Campus (the University) and its affiliated health systems have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver | Anschutz Medical Campus
- University of Colorado Health
- The University of Washington
- Case Western Reserve University (for the sleep sub-study)
- The University of Alabama at Birmingham

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

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The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

*Kristine Erlandson, MD
12700 E. 19th Avenue, Mail Stop B168
Aurora, CO 80045*

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- The Institutional Review Board that is responsible for overseeing this research
- The study doctor and the rest of the study team.
- The National Institutes of Health, who is the organization paying for this research study.
- Officials at the institution where the research is 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

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.

You have the right to request access to your personal health information from the Investigator.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available to investigators at the other study sites, University of Washington and University of Alabama. We will share the data with investigators involved with The Health Study at those institutions, but will not share any information that would identify you. If you agree to participate in the optional sleep sub-study, only sleep data, medical history, demographic information and blood sample will be shared with a researcher at Case Western University. We will not share any information that would identify you.

Some of the research procedures involve genetic testing or the use of your genetic information. Your genetic information will be released to databases, as required by the National Institutes of Health, but this information will not be linked to you or any other people in the study:

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Psychological and mental health tests
- Alcoholism, Alcohol or Drug abuse
- Testing for or infection with diseases reportable to the Public Health department, including but not limited to: Human Immunodeficiency Virus (HIV), hepatitis (all forms) tuberculosis, or other sexually transmitted diseases.

Combined Biomedical Consent and Compound HIPAA authorization
CF-151.C, Effective 06-20-19

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- Tissue samples and the data with the samples.

What happens to Data, Blood and Tissue Specimens that are collected in this study?

Scientists at the University and the health systems involved in this study work to find the causes and cures of disease. The data, blood and tissue specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, blood, and other tissue specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, blood, or other tissue specimens collected from you.
- If data, blood, or other tissue specimens are in a form that identifies you, the University or the health systems involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures

In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above. Some of these optional procedures may involve genetic testing or the use of your genetic information. Your genetic information will be released to the NIH repositories, but will not be linked to you.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature: _____

Date: _____

Print Name: _____

Consent and Authorization Form

Consent form explained by: _____

Date: _____

Print Name: _____

Consent and Authorization Form

COMIRB
APPROVED
For Use
03-Oct-2024
23-May-2025

Principal Investigator: Allison Webel, PhD, RN

COMIRB No: 19-1985

Version Date: 9/27/2024

Study Title: The HEALTH Study

Key Information:

Please read all the information below and ask questions about anything you don't understand before deciding if you want to take part.

You are being asked to be in a research study. Participation in research is voluntary.

Purpose of this study: The purpose of this study is to learn more about what types of exercise has the best results with regards to improvement in muscle function and decrease in fatigue and what helps people aging with HIV continue to exercise on their own.

Procedures: If you agree to participate, the following will happen:

- There are 3 visits in the Screening phase to see if you are eligible for the study. If you qualify and want to continue to participate, you will be randomly assigned to 1 of 2 different types of exercise (Continuous Moderate Intensity or High Intensity Interval training). You do not get to choose which arm of the study you are in.
- Participation in the exercise phase involves exercising in either our exercise center or a recreational center 3-4 days/week for about 4 months (16 weeks) and then an additional 3 months of exercising on your own. Total participation in the study could be up to 9 months.
- If you agree to participate, you will be asked to be in optional parts of the study, including an extra follow up visit at the end (12 month follow up).

Risks: Participation in this study involves risks, including the following:

- Muscle and joint pain, alteration in heart rate, changes in blood pressure, healthcare exposures (risk of exposure to infection) due to exercising around others, exposure to radiation, pain/bruising from blood draws/muscle biopsies, being tired or bored during tests of thinking abilities, dizziness/lightheaded from exercise/blood draws/fasting, claustrophobia from MRI.

Benefits: There is no guarantee that your health will improve if you join this study. This study may lead to information that could help patients and health care providers in the future.

Detailed Consent:

Why is this study being done?

This study plans to learn more about how exercise changes muscle strength and muscle function in people aging with HIV.

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Exercise has many beneficial effects, including an improvement of muscle function with aging. We don't know the best kind of exercise for people with HIV. We also don't know how we can best help people continue exercising long term. The purpose of this study is to:

1. Test which type of exercise leads to the biggest improvement in muscle function and reduction in fatigue.
2. See what helps people keep exercising on their own, after exercising in a gym with a trainer.
3. Optional sleep sub-study- Test which type of exercise leads to the biggest improvement in sleep quality.

You are being asked to be in this research study because you are aging with HIV and are not currently exercising regularly.

Other people in this study

Up to 100 people from your area will participate in the study.

Up to 300 people around the country will be in the study.

Sleep sub-study approximately 50 people from your area.

What happens if I join this study?

If you join the study, we must find out if you meet the study requirements.

Initial screening visit

- At the initial screening visit, you will answer several questions about your medical problems and medications you take. You will complete a few surveys.
- You will have your blood pressure, height, and weight measured.
- Then you will have an exercise test to find out if your heart is healthy. This will involve walking or running on a treadmill for about 10 minutes. You will breathe through a special mouthpiece during this test. The exercise will be easy at first, but will gradually become more difficult until you can no longer continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal.

Screening visit 2 ,3, and 4

- You will have a blood draw
 - * There is a possibility that blood work may need to be repeated or redrawn at a subsequent screening visit if there is a problem with the sample.
- We will measure your muscle function through several tests and measure body composition using DXA scan
- A urine pregnancy test will be administered prior to a DXA scan for women who are currently still menstruating
- You will also have the option of completing a muscle biopsy and MRI/MRS scan.
- You will also have the option of completing some tests and surveys on your thinking and daily abilities.
- *If you meet the requirements* and want to continue to take part in the study, you will:

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- 1) Be assigned randomly (a process similar to flipping a coin) to 1 of 2 different types of exercise: continuous moderate intensity or high intensity interval training.
- 2) Exercise regularly in our exercise center or similar exercise facility 3 to 4 days per week for about 4 months (16 weeks). The facility will need to meet certain criteria and will need to be approved by the research team.
- 3) Be assigned randomly to 1 of 2 different types of follow-up: more intensive or less intensive text messaging.
- 4) Complete an additional 3 months of exercise on your own.
- 5) Be asked to be in optional parts of the study
- 6) Have the option to participate in interviews to tell us how exercise is going and your thoughts about exercise.
- 7) Have several visits to test your muscle function and complete surveys throughout the study.
- 8) Have a post-exercise research visit. This visit will include the option to complete a 2nd muscle biopsy.
- 9) Complete a visit after the study is over to check-in (12 months after starting exercise).

The above procedures will take about 7 months. With the time for screening and completing study visits, the total time that you are involved with the study may be up to 9 months. If you choose to do the additional follow-up, your time in the study may be up to 14 months.

Here, we will describe in more detail what the study will involve. Please be sure to ask questions if you have any:

- 1) **Exercise program-** The goal of the exercise program is to build muscle mass and improve your ability to exercise over 4 months. You will come to our exercise center or similar facility 3 to 4 days a week. Each session will take about 1 ½ hours.

You will do a variety of exercises that build muscle mass, such as walking, jogging, and weight lifting. You will start at a lower intensity while you learn the exercise, but the goal will be to gradually increase to a more moderate or intense exercise. For each exercise session, you will have a list of exercises for the day. You will write down information on what you complete (exercise log).

You will continue to exercise after the first 4 months at a place that you chose. This could be at your home, outside, or at a gym.

- 2) **Research Tests**— The research tests are shown on the table below. Most of the research tests will be completed at a Pre-Exercise and a Post-Exercise Visit. These visits will last up to 3 hours (if you chose to have a muscle biopsy), or about 2 ½ hours if you do not have a muscle biopsy. All of the tests are done for research purposes and all are voluntary.
 - ***Exercise capacity-*** This will involve walking or running on a treadmill for about 10 minutes. You will breathe through a special mouthpiece during this test. The exercise will be easy at first, but will gradually become more difficult until you can no longer continue. We will monitor your heart activity (ECG) and blood pressure during the test to make sure they are normal. In addition to the screening visit, you will also have this after about 4 months (week 16).
 - ***Muscle biopsy (optional)***— This test involves taking a small piece of leg muscle so that we can try to learn how exercise changes the muscle. You will be asked to abstain from alcohol or caffeinated beverages (coffee, cola, etc) after 1:00 p.m. the day prior, and to fast from any food or drink beginning at 9 p.m. with the exception of water and medications. You will arrive the following morning for the biopsy. After getting numbing medicine (lidocaine), a small cut (about one-quarter of an inch) is made in your thigh and a small piece of muscle is removed. This takes about 60 minutes.

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- **MRI/MRS (optional)** – This involves lying flat in the MRI machine for less than 45 minutes at a time for up to 2 sessions. You will be asked to avoid vigorous activity for 2 days prior to the scan. You will be asked to push your foot against a pedal for 90 seconds and then to relax for 8 minutes. The MRI will scan your left thigh and calf. The visit may last up to about 2 hours, allowing time to change clothes and scanners.
- **Stool Collection (optional)**- This involves collecting a small sample of your stool (poop). We will provide you with a device you can place under the toilet seat to collect the stool. You will use a wooden stick to transfer some of your stool to a collection cup. The sample cup will be stored in your freezer in paper bag until you come for your next research visit. The device to collect the stool and the stick are thrown into the trash.
- **Blood tests** – We will draw between 2 and 5 tablespoons of blood at up to 4 of the visits. These visits will be in the morning after an overnight fast (nothing to eat or drink except water, for 8 hours).
- **Activity monitor** – For 1 week at the beginning, the middle, and monthly during Part 2 of the study, you will wear a small monitor that records your activity. You will need to bring the monitor and log with you to your next visit.
- **DXA scan** – This test will measure your muscle, fat, and bone. The test involves lying still on a table for about 30 minutes.
- **Interviews (optional)** —At up to 4 visits, if you agree to participate, one of our research team members will have a one-on-one discussion with you about your thoughts on the study, on your ability to keep exercising, and about how you feel with exercise. If you decide to decline participation before starting exercise or withdraw from the study, a decline/withdrawal interview may be offered to you to determine your reasons behind your decision and/or ways to improve the study intervention. This meeting will be held in a private setting (an exam room, phone, or by secure zoom), and will be audio-recorded. Your name and identifying information will not be recorded.
- **Physical function** – These tests will include 1) the time to rise from a chair 10 times without using your hands, 2) the time it takes you to walk 400 meters (about 400 yards), 3) the time it takes you to walk 4 meters, and 4) a balance test, and 5) grip strength. These tests will take about 20-30 minutes for all of the testing, which will be measured at baseline, week 16, and the end of the study. Two of the tests will be measured once a month (will occur at the research center).
- **Muscle strength** - For this test you will start with light weights and gradually try to lift heavier weights until you feel that you have lifted as much weight as you can using proper lifting form. This test takes about 1 hour. You will do this in place of one of your regular exercise training visits (will occur at the research center).
- **Surveys**—Throughout the study, you will complete several paper surveys on your fatigue, activity, and sleep. The time to complete these surveys will be about 20-30 minutes. In addition, you will record what you eat for 3 days at the beginning of the study and again after part 1 (after about 4 months of exercise). At the 12-month visit you will complete some surveys through text messaging. We will send a text message to your phone with a link to complete a survey in the morning and in the evening for 7 days.
- **Health Status**- Once per month while you are exercising, we will ask you to complete a form regarding any changes in your medical history. Although you will notify us using this form, *please be sure to let us know right away when you have had any changes in your medications, visits to the doctor, or any other changes.*
- **Tests on thinking abilities (optional)** — at up to 4 visits, we will ask you to complete some tests that measure how quickly you think, your ability to solve problems, and your memory. For some of these tests your responses will be audio-recorded. Your name and identifying information will not be recorded. This should take about 1 hour.

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						Part 1 Week Number						Part 2 Week Number				12 month follow-up (optional)
Test	Screen#1	Screen#2	Screen#3	Screen#4	0	2	4	8	12	16	End Part 1	4	8	12	End Part 2	48*
Exercise capacity	X									X						
Muscle biopsy*		X									X					
MRI/MRS*				X							X					
Blood draw		X								X						X
Wear activity monitor		X									X	X	X	X		X
Collect stool sample*		X									X					
*Microbiome Questionnaire		X									X					
Urine Pregnancytest (if menstruating)			X								X					
DXA scan			X								X					
Interviews*			X								X				X	X
Physical function*			X		X		X	X	X	X	X	X	X	X	X	
Muscle strength**						X	X	X	X	X	X				X	
Fatigue questions*			X		X		X	X	X	X	X	X	X	X	X	
Other surveys			X								X				X	X
Health status					X		X	X	X	X		X	X	X	X	
Thinking ability tests*		X										X				X

*optional test; optional visit done 12 months after starting the intervention (part 1 of study).

** Muscle strength, physical function, and fatigue questions will be assessed every 2-4 weeks. These will occur either just before/after or during a regular exercise session and will not require an additional visit.

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Optional Sleep sub-study- Screening Visit #1: Consent, medical history and sleep survey administration.

Consent: After obtaining informed consent, the first of two baseline visits will include medical history, Resironics actiwatch initiation, provide sleep diary and sleep survey administration (Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance). Please note, the medical history, PSQI and PROMIS SF are already collected as part of the ongoing HEALTH study.

Actiwatch Initiation and Sleep Diary: The RA will initialize the participant's actiwatch and instruct each participant on proper use of the actiwatch (Phillips Respironics Actiwatch Spectrum Plus). During initialization the RA will enter all required demographic information. If a participant is transgender, sex assigned at birth should be used, as the variable of sex does not impact the data. Participants will be asked to wear the device for 10 consecutive days at baseline and again post 16-week intervention. The actiwatch, which resembles a wristwatch and is worn on the non-dominant wrist. The device should be fully charged. While wearing the actiwatch, participants will be instructed to complete a corresponding **10-day sleep diary** that will collect information including time each participant went to bed, wake time, time out of bed, how many times they awoke during the night, and naps taken during the day. This information will be used to score the actiwatch data to determine our primary outcome, sleep quality. Collected data will include weekday and weekend days in the 10-day period of time. Participants should be instructed to wear the actiwatch for 10 days, 24hours per day, except when bathing or swimming.

Sleep Surveys: Sleep quality and patterns of sleep will be evaluated using the validated Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance. The PSQI measures seven domains of sleep: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction over the last month. The PROMIS Short Form –Sleep Disturbance measures sleep disturbance during the past week.

Screening Visit #2 (approximately 8 days' post baseline visit 1): Fasting blood draw after refraining from exercise for ≥ 48 hours, return actiwatch and sleep diary, and sleep survey administration.

Blood Draw: A fasting blood draw will be taken at the beginning of the second baseline visit, collected between 6:30 – 10:00 am. The participant should refrain from exercise for ≥ 48 hours. The clinical blood draw should include:

- 10 ml K2EDTA tube (plasma will be collected for analysis for inflammatory markers)

The primary inflammation markers of interest are IL-6, IL-10, IL-13, IFN- γ , CRP and TNF- α due to prior association with sleep quality, other inflammation markers, IL-1 β , IL-2, IL-4, IL-8 and IL-12p70 will be exploratory to identify potential pathways of sleep impairments.

Sleep Surveys: The Pittsburgh Sleep Quality Index (PSQI) and PROMIS Short Form –Sleep Disturbance forms should be completed to measure sleep quality and patterns of sleep.

Return of actiwatch and sleep diary (approximately 10 days after screening visit #2): The RA will collect the actiwatch and sleep diary from the participant. The RA will check wear time for the actiwatch. If the participant did not meet wear time criteria (wearing the device for ten days), the RA will ask the participant if they are willing to wear the device again for approximately ten days. If they are willing to re-wear the device, the participant should be reinstructed on proper use and wear time criteria and provide the participant with a new sleep diary. The RA should also check the sleep diary for completeness. If the participant did not complete or has missing data in the diary the RA should assist the participant with completion of any missing data, if possible.

Intervention Week 8 Visit (midpoint of intervention): Fasting blood draw after refraining from exercise for ≥ 48 hours and sleep surveys. The procedures are described above.

Intervention Week 16 Visit (completion of intervention): Fasting blood draw after refraining from exercise for ≥ 48 hours, actiwatch initiation, sleep diary and sleep survey administration. The procedures are described above.

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End of Study Visit: Return actiwatch and sleep diary. The procedures are described above.

Sleep sub-study tests	Screening visit #1	Screening visit #2	10 days post screening visit #2	Intervention Week 8 visit	Intervention Week 16 visit	End of study
Actiwatch initiation		X			X	
Actiwatch return		X	X			X
Sleep diary initiation		X			X	
Sleep diary return		X	X			X
Sleep surveys	X	X		X	X	
Blood draw		X		X	X	

What are the possible discomforts or risks?

- **Exercise testing, exercise training, strength tests, physical function tests** – When you exercise, there is a chance that you will feel pain in your muscles or joints, feel dizzy or faint, have irregular heartbeats, have low or high blood pressure, have a slow or fast heart rate, have a stroke or heart attack, or die. The risk of death from an exercise test has been estimated to be 1 in 100,000. The risk of a heart attack is about 4 in 10,000 and the risk of a problem that would require hospitalization (for example, chest pain) is about 2 in 1,000.
- **Healthcare exposures** - Your research visits and exercise sessions will be conducted in a building with other staff and study participants. We will take all precautions to minimize your risk for exposure to any infections, including but not limited to COVID-19. To limit exposures, you should wear a mask when coming into the research center, wash your hands with soap and water regularly, and avoid coming to visits if you have any symptoms of an infection such as COVID-19, including fever, cold symptoms, loss of taste or smell, shortness of breath. You should also call your study team and stay home if you have a known or possible exposure to someone with COVID-19. This risk may be higher at other facilities.
- **DXA scans** – As part of this study we will perform DXA scans of your total body. A DXA is a way of looking inside your body using X-rays. X-rays are a type of radiation. Everyone gets some radiation from their environment every day. The total radiation dose you will receive from the DXA is less than the amount of radiation that you would receive from your environment 1 day. This radiation dose involves minimal risk and is necessary to obtain the research information desired.
- **Blood tests** – Throughout the study, we will need to get a total of up to 17 tablespoons of blood from you over 9 months. If we need to repeat some of the blood tests, this may increase to about 20 tablespoons. We will get blood by putting a needle into your veins and letting the blood flow into a plastic 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 your skin.
- **Fasting**—You will be asked to avoid drinking anything other than water and avoiding eating anything after midnight until blood draw or muscle biopsies are completed on some of the visits. Fasting, or not eating for a period of time, can sometimes make you feel tired, dizzy, lightheaded, or even nauseous. Drinking plenty of water, ensuring you have a regular meal the evening before, and holding diabetes medicines until you have eaten (if diabetic) can help to minimize these symptoms.
- **Muscle biopsy (optional)** – In this study we will need to take 2 small samples of your leg muscle. This procedure is called a “biopsy”. Before we take the samples, we will give you some medication to numb the area. We will then make a small cut in the skin and take the samples by pressing a hollow needle into your muscle. When we take the needle out, it will remove a small circle of muscle called a “plug”. There are some risks to taking a sample of muscle this way. During the biopsy you may feel some pain. Tenderness and bruising at the tissue sampling site is common, and this can sometimes last several days. There is a small chance that you could get an infection where the needles goes in. There is also a small chance that you

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could have an allergic reaction to the numbing medicine. After your skin heals up, you will have a small scar where we take the sample.

- *MRI and MRS (optional)* – You may develop claustrophobia in the magnet or a mild muscle cramping during the exercise portion of the scan. You will not be able to perform the scan if you have an implanted devices (i.e. pacemaker or insulin pumps). The MRI machine may also be loud, you will be provided with ear plugs to help increase comfort.
- *Stool sample (optional)* - You might feel uncomfortable or embarrassed collecting your stool sample. You will be provided with gloves and all of the needed equipment to minimize any contact with the sample. We encourage you to wash your hands thoroughly after collecting the sample.
- *Activity monitor*- This is a small device that you will wear continuously during the day. This can be bothersome to make sure that you always have your monitor with you.
- *Surveys*—You may feel embarrassed or uncomfortable when answering some of the survey questions.
- *Tests of thinking abilities* -- You may feel tired or frustrated during the tests of thinking abilities. No one does well on all the tests. You can stop at any time.
- *Confidentiality and privacy*: You may feel embarrassed when answering any of the questions for this study. We will do all that we can to protect your information. Any information that you share with the researcher involving use of illegal substances (such as cocaine or other drugs) will be protected. But there are some things we cannot keep private. If you give us information about hurting yourself, we will refer you immediately to a provider in the clinic or the Emergency Department. If you give us information about someone hurting someone else, we have to report that to the police. If you have a new diagnosis of HIV during the study, we will have to notify the health department. Finding out you have HIV may make it hard for you to get insurance. If a court orders us to hand over your study records, we have to hand them over to the court. There is a risk that people outside of the research team will see your research information.
- This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. The Certificate prohibits the researchers from disclosing your name, or any identifiable information or document from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings. These protections apply only to your research records. The protections do not apply to your medical records. The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:
 - To those connected with the research,
 - If required by Federal, State or local laws,
 - If necessary for your medical treatment, with your consent,
 - For other scientific research conducted in compliance with Federal regulations,
 - To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or
 - Under other circumstances with your consent.
- The study may include risks that are unknown at this time.

What are the possible discomforts or risks in the optional sleep sub-study?

- *Blood tests* – We will collect 10 milliliters or approximately 2 teaspoons of blood from you. We will get blood by putting a needle into your veins and letting the blood flow into a plastic 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 your skin.
- *Fasting*—You will be asked to avoid drinking anything other than water and avoiding eating anything after midnight until the blood draw is completed on some of the visits. Fasting, or not eating for a period of time, can sometimes make you feel tired, dizzy, lightheaded, or even nauseous. Drinking plenty of water, ensuring you have a regular meal the evening before, and holding diabetes medicines until you have

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eaten(if diabetic) can help to minimize these symptoms.

- **Actiwatch-** This is a small device that you will wear continuously during the day and at night. This can be bothersome to make sure that you always have your monitor with you.
- **Surveys**—You may feel embarrassed or uncomfortable when answering some of the survey questions.
- **Confidentiality and privacy:** You may feel embarrassed when answering any of the questions for this study. We will do all that we can to protect your information. But there are some things we cannot keep private. If you give us information about hurting yourself, we will refer you immediately to a provider in the clinic or the Emergency Department. If you give us information about someone hurting someone else, we have to report that to the police. If you have a new diagnosis of HIV during the study, we will have to notify the health department. Finding out you have HIV may make it hard for you to get insurance. If a court orders us to hand over your study records, we have to hand them over to the court. There is a risk that people outside of the research team will see your research information.
- The study may include risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for the research team to learn more about the type of exercise that leads to the most improvement in muscle in people with HIV. The study will also help the research team know the best ways to help people keep exercising. The Sleep sub-study is designed to learn more about the type of exercise that leads to improved sleep quality in people with HIV.

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 by the National Institutes of Health.

Will I be paid for being in the study?

- You will be compensated for your participation in this study. The payments will be combined and provided by a check 1) after the screening is completed, 2) after week 16 (End of part 1), 3) at the end of the main study (end of part 2), and 4) if you complete the optional visit 12-month visit.
- You will be paid \$50 if you complete the entire first screening visit.
- You will be paid \$35 for the second screening visit (*including wearing and returning the activity monitor*).
- You will be paid \$35 for the third screening visit.
- You will be paid \$75 each time if you complete the optional thinking tests (up to 3 times during the main study visits).
- You will be paid \$150 for each muscle biopsy visit (one at the beginning and one at week 16 - end of part 1).
- You will be paid \$100 for each MRI/MRS visit (one at the beginning and one at week 16 - end of part 1).
- You will receive \$25 for each of the in-person physical function and fatigue checks during the second part of the study (3 total). You will receive \$50 for completing the week 16 visit (*including wearing and returning the activity monitor*).
- You will receive \$50 for the final main study visit (*including wearing and returning the activity monitor*).

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- You will receive \$125 for completing an optional visit approximately 12 months after you start exercise (including wearing and returning the activity monitor, and responding to most of the text message surveys)..

This will add up to a total of \$1145 if you complete all of the visits, including both muscle biopsies, MRI/MRS scans, thinking ability tests, and the 12 month follow up. This will add up to a total of \$295 if you complete all the visits, but do not have the muscle biopsies, MRI/MRS scans, thinking ability tests, and the 12 month follow up.

If you decide to complete the intervention at an approved exercise center, fees will be paid directly to the facility.

If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed. It is important to know that payment for participation in a study is taxable income.

Transportation and parking assistance

- For the exercise sessions: You will be compensated for every exercise session that you attend (during week 1 to week 16). You will be paid \$5 for every exercise session as transportation assistance and the payments will be combined and provided to you at the end of every week. This will add up to \$240 if you complete all of the exercise sessions. If you leave the study early, you will be paid only for the exercise sessions you have completed. Parking for the exercise sessions will be free.
- For the optional MRI/MRS visit: You will be paid \$25 for each MRI scan that you attend as transportation and parking assistance. This will add up to \$50 if you attend both MRI/MRS visits (one at the beginning and one at week 16 - end of part 1).

Sleep Sub-study

- You will be paid \$20 for the first screening visit
- You will be paid \$35 for the second screening visit, \$20 for completion of the fasting blood draw and sleep surveys and \$15 for return of the completed Actiwatch and sleep dairy.
- You will be paid \$20 for the completion of blood draw and sleep surveys at the intervention week 8 visit.
- You will be paid \$20 for the final end of study visit (including wearing and returning the Actiwatch)

*This will add up to \$95 if you complete all of the sleep sub-study visits. If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed. It is important to know that payment for participation in a study is taxable income.

Will I have to pay for anything?

It will not cost you anything to be in the study, other than the costs of traveling to and from our facility. However, if one of the medical tests (for example, the treadmill exercise test) reveals a potential health problem that requires further evaluation, you will need to be cleared by your own health care provider if you want to take part in the study. *This may lead to added costs to you or your insurance company. You are encouraged to ask questions about these possible costs.*

In the second half of the study, we ask that you continue exercising. We may also provide you with some tools such as educational materials and an activity monitor to help you do this.

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 you leave this study, you will still receive your normal medical care. 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.

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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?

If you have an injury while you are in this study, you should call Dr. Allison Webel (the NIH Research Principle Investigator) immediately. Her phone number is 216-368-2912. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Dr. Allison Webel. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Webel at 216-368-2912. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Webel with questions. You can also call the University of Washington Institutional Review Board (MIRB). You can call them at 206-543-0098. 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.

Optional Components of the Study (Muscle biopsy, stool collection, interviews, sleep sub-study)

- If you decline to participate in these portions of this study, you cannot take part in these optional procedures, but you can still participate in the main study. Please state if you agree or not to the optional procedures and insert your initials.

1. Do you agree to participate in the **muscle biopsy** portion of the study?

☐ Yes ☐ No _____ Initials

2. Do you agree to participate in the **stool collection** portion of the study?

☐ Yes ☐ No _____ Initials

3. Do you agree to participate in the **interview** portion of the study?

☐ Yes ☐ No _____ Initials

4. Do you agree to participate in the **sleep study** portion of the study?

☐ Yes ☐ No _____ Initials

5. Do you agree to participate in the **MRI/MRS** portion of the study?

☐ Yes ☐ No _____ Initials

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6. Do you agree to participate in the **tests of your thinking abilities**?

☐ Yes ☐ No _____ Initials

7. Do you agree to participate in the **12-month follow up** portion of the study?

☐ Yes ☐ No _____ Initials

Optional Consent and Authorization for Data and Specimen Banking for Future Research

Dr. Webel would like to keep some of the data, blood and tissue that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about muscle, aging, and exercise in people with HIV. The research that is done with your data and samples is not designed to specifically help you. It might help people who have HIV and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Webel keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want her to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Webel decides to destroy them.

When your data and samples are given to other researchers in the future, Dr. Webel will not give them your name, address, phone number or any other information that will let the researchers know who you are.

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 data and samples include learning more about what causes muscle weakness with aging and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. Webel 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 Dr. Webel.

Please read each sentence below and think about your choice. After reading each sentence, circle "yes" or

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“no.” 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, blood and tissue to be stored in a central tissue bank at The University of Colorado for future use by the study investigators:

8. I give my permissions for my data, blood and tissue samples to be kept by Dr. Webel for use in future research to learn more about how to prevent, detect, or treat muscle weakness with aging.

☐ Yes ☐ No _____ Initials

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

☐ Yes ☐ No _____ Initials

10. 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

Who will see my research information?

The University of Colorado Denver | Anschutz Medical Campus (the University of Washington) and its affiliated health systems have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver | Anschutz Medical Campus
- University of Colorado Health
- The University of Washington
- Case Western Reserve University (for the sleep sub-study)
- The University of Alabama at Birmingham

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Allison Webel, PhD, RN

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Box 357260
University of Washington
Seattle, WA 98195

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- The Institutional Review Board that is responsible for overseeing this research
- The study doctor and the rest of the study team.
- The National Institutes of Health, who is the organization paying for this research study.
- Officials at the institution where the research is 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

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.

You have the right to request access to your personal health information from the Investigator.

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available to investigators at the other study sites, University of Colorado Denver | Anschutz Medical Campus and University of Alabama. We will share the data with investigators involved with The Health Study at those institutions, but will not share any information that would identify you. If you agree to participate in the optional sleep sub-study, only sleep data, medical history, demographic information and blood sample will be shared with a researcher at Case Western University. We will not share any information that would identify you.

Some of the research procedures involve genetic testing or the use of your genetic information. Your genetic information will be released to databases, as required by the National Institutes of Health, but this information will not be linked to you or any other people in the study:

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Psychological and mental health tests
- Alcoholism, Alcohol or Drug abuse
- Testing for or infection with diseases reportable to the Public Health department, including but not limited to: Human Immunodeficiency Virus (HIV), hepatitis (all forms) tuberculosis, or other sexually transmitted diseases.
- Tissue samples and the data with the samples.

What happens to Data, Blood and Tissue Specimens that are collected in this study?

Scientists at the University and the health systems involved in this study work to find the causes and cures of

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disease. The data, blood and tissue specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, blood, and other tissue specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, blood, or other tissue specimens collected from you.
- If data, blood, or other tissue specimens are in a form that identifies you, the University or the health systems involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures

In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above. Some of these optional procedures may involve genetic testing or the use of your genetic information. Your genetic information will be released to the NIH repositories, but will not be linked to you.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature: _____

Date: _____

Print Name: _____

Consent form explained by: _____

Date: _____

Print Name: _____