



INFORMED CONSENT DOCUMENT

Project Title: Exercise Training to Improve Brain Health in Older HIV+ Individuals

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This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form, you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are a person 40 years of age or older who has been infected with HIV.

The purpose of this research is to study:

1. The effect of exercise on cognitive functioning in older individuals with HIV.
2. The effect of exercise on brain structural and functional measures.

The majority of people living with HIV are now over 40 years old. Attempts to better these individuals' quality of life (especially memory and thinking abilities) have largely been unsuccessful through medication management alone. This study will offer a structured exercise regimen as an additional treatment to the current standard of care in the hopes of improving brain health of older individuals living with HIV.

WHAT WILL HAPPEN DURING THIS STUDY?

To be eligible for the study:

- you must have a documented history of HIV infection
- your HIV must be well-controlled on stable cART regimens for approximately 3 months prior to enrollment
- you must be able to have an MRI
- you must not exercise more than approximately 2 hours/week
- you must not have engaged in regular exercise for approximately 3 months prior to enrollment.
- you must be willing to wear a mask at all times when on the medical school campus.

For all participants, to determine your eligibility, you will have a screening evaluation, which includes:

1. Urine pregnancy tests (done on the day of the scan AND the day of cardiorespiratory capacity testing, if not completed on the same day and only for females with no documented history of sterilization, menopause, etc.)
2. A urine drug screening test for cocaine, amphetamines, methamphetamine, barbiturates, benzodiazepines, marijuana, opiates, PCP, methadone, and tricyclic antidepressants, such as amitriptyline or nortriptyline. A positive result will not necessarily exclude you from the study.
3. The Neuroimaging Screening Form, which asks questions about your feelings about being inside a closed space like the MRI scanner, questions about history of head injuries, and questions about any metal that subjects may have implanted in your body or any metal piercings that cannot be removed.
4. A Locator Form with your basic contact information, as well as additional names of people who might also be able to contact you should you be lost to follow up. When asking for your zip code on this form, we will use it not only to contact you, but also to determine the median income for the area in which you live.
5. HIV Dementia Scale (HDS) – This assessment will screen you for memory and attention deficits, as well as psychomotor slowing.
6. Center for Epidemiologic Studies Depression Scale (CES-D) – A self-reported questionnaire to assess symptoms of depression.
7. Scanning Cover Sheet – You will be asked questions about your demographics and other basic information, such as age, race, gender, handedness, years of education, first language, height/weight, date of HIV diagnosis (and date started medications if applicable), as well as information about drug, alcohol, tobacco and caffeine use. When asking for your zip code on this form, we will use it not only to contact you, but also to determine the median income for the area in which you live.
8. You will also be asked to sign a Release of Information form so we can obtain your medical records, including but not limited to medical, hospitalization, HIV, STD, substance use/abuse/dependence and mental health records from your doctors, results from prior blood, diagnostic, imaging and laboratory tests and other information obtained from interviews or questionnaires related to your medical care. We may also review the records of any Washington University research study in which you participate. This will allow us to better determine your eligibility, insure and improve your safety, and decrease your burden if the results of tests done in one research study could be used as data for another instead of asking you to unnecessarily repeat a procedure.
9. We will review your medical history and records related to any of your HIV/AIDS-related outpatient visits, inpatient hospitalizations, blood/diagnostic/laboratory/imaging tests (such as CD4 count, viral load, nadir CD4 count, duration of infection, thyroid and liver function, creatinine, c-reactive protein, complete blood counts studies, total fasting cholesterol with LDL/HDL and triglycerides, fasting

glucose, and glycosylated hemoglobin, STD history, AST, ALT, fibrinogen-4, GFR, platelets, HCV, IL-6, d-dimer, hsCRP, and any other HIV- or inflammatory-related labs deemed necessary; any abnormal/exclusionary imaging results, etc.), substance use/abuse/dependence, and mental health treatment. Additional information may also be obtained from clinical interviews or questionnaires found in your records related to your medical care. We may also review your research records from other WUSM studies (to see if previous results indicate any exclusionary criteria or provide any results that we could use as data for this study so as to not have you repeat procedures and decreasing your burden whenever possible). These records will only be accessed as long as necessary to acquire study data.

If, on the basis of these tests and at the PI's discretion, you are eligible to continue in the study, you will be asked to complete the following study procedures. The Screening Evaluation and Baseline Assessments can be completed on the same or separate days.

BASELINE ASSESSMENTS:

1. Neuropsychological (Memory) Tests -- These are exercises that are related to memory, how fast you do things with your hands, and how you pay attention to tasks. There are a number of different tasks; some are timed and some are not. These will take approximately 1-1½ hours to complete.
2. Questionnaires regarding your mood, ability to care for yourself, as well as your drug and alcohol history. These will take approximately ½-1 hour to complete, and you may skip any questions that make you feel uncomfortable.
3. Neuromedical and physical examination -- A doctor will examine the nerves in your face, as well as test your reaction to touch and will test the reflexes in your arms and legs. We will check your waist circumference, height, weight, take your vital signs (blood pressure, heart rate, respiration, etc.), and also perform a regular physical. This will take approximately 20 minutes.
4. Cardiorespiratory capacity testing (the ability of your heart and lungs to supply oxygen to your muscles during sustained physical activity): You will have a detailed cardiovascular evaluation (described below), which will take place in the Cardiovascular Imaging and Research Laboratory. You will be asked to fast overnight for 10-12 hours before the cardiovascular testing, and not to take any diabetes medications in the morning to prevent low blood sugar during the screening visit. You may drink water and take your prescribed medications (unless instructed otherwise by the research study team). You will be asked to not take any beta-blockers, calcium channel blockers with nodal blocking effects (i.e., non-dihydropyridines) or other blood pressure drugs known to suppress heart rate the morning of the testing. We will review your medications with you so that you know which ones need to be held for this study. An intravenous line may be placed in your arm vein. This line will be kept in place for several hours during the cardiovascular evaluation (described below).

Out of an abundance of caution to avoid the spread or contraction of COVID-19, when you arrive for testing, you will be required to wear a special mask, face shield or goggles, gloves, and/or a disposable gown. The staff will be wearing similar personal protective equipment.

We will share the results of this testing with you.

The following tests will be done:

a. Resting and Exercise Stress Echocardiogram, and exercise fitness test. You will undergo a resting echocardiogram, which will be followed by an exercise stress echocardiogram and an exercise fitness test.

The stress tests will take place in the Cardiovascular Imaging and Research Laboratory and will be supervised by experienced technicians/nurses and a physician. This test uses sound wave pictures of the heart (echocardiogram) to obtain information about your heart and its response to exercise. Small adhesive patches are applied to your chest to record the electrical activity of your heart.

You will be asked to exercise on a stationary bicycle for the exercise stress test. During this test, you will breathe through a mouthpiece which is connected to a machine that measures how many calories your body uses during exercise. Exercise will be started by pedaling at a constant rate with minimal resistance. After a short warm-up period, the resistance will be increased every 1-2 minutes until you reach your maximum heart rate and are too tired to continue, or you experience some other limiting factor, such as chest pain or other discomfort. Typically, the exercise test lasts 3 to 12 minutes depending on your level of physical fitness. At rest and at 2-3 minute intervals during this exercise test, your heart rate and rhythm will be monitored using an electrocardiogram, and your blood pressures will be monitored using a cuff placed on your upper arm and a (possibly) stethoscope placed in the front area of your forearm. The technician and/or physician supervising the test may stop the exercise at any time for your safety.

You will be asked to complete a 6-minute walk for the exercise fitness test, so make sure to wear comfortable clothing and walking shoes. During this test, you will walk as far as possible during 6-minutes. Timing starts when you are instructed to "Go." You will then walk back and forth in a straight line and go around two markers, such as cones, which are 30 meters (100 feet) apart. If you get tired during this test, you may slow down, stop, and rest as necessary, then start walking again as soon as you are able. The person supervising the test will let you know how much time has passed every minute. The technician and/or physician supervising the test may stop the exercise at any time for your safety.

b. Body composition assessment. You will have a DXA (Dual energy X-ray absorptiometry) scan to evaluate how much body fat and lean tissue you have and where your body fat is located. This test involves lying on a table for about 10 minutes while the machine scans your body. It will measure your total body fat and lean mass, and bone mineral density.

5. We will also review your medical history and records including any physical exam reports, laboratory and imaging results.

6. We will attach a small device (an activity meter, like a watch) that measures your day-to-day activity and rest to your non-dominant wrist or ankle. You will wear the device for approximately 2 weeks before and 2 weeks after the intervention. You may also be asked to wear it for some duration of the intervention, from 1 week to throughout the entire intervention. You will not be able to remove the activity meter until we remove it for you upon your return for the last follow-up appointment.

Periodically throughout the study, your de-identified data will be downloaded onto a secure computer/external hard drive. Only members of the research team will be able to see this data, and your name will never appear on it. You will also be asked to complete a daily sleep diary whenever you are wearing the activity meter.

7. Fasting labs: We will ask you to fast (not have anything to eat or drink other than water) overnight (approximately 10-12 hours) and then draw some of your blood to look at the amount of fat and sugar in your body, as well as markers of inflammation and insulin resistance. The blood draw will be done by staff of either the ACTU, ID Clinic, Barnes or Quest Laboratory, or the Center for Clinical Studies (CCS) and will be equivalent to approximately 9 tablespoons, including blood samples taken to determine if you are a carrier of the *Apolipoprotein E (ApoE) ε4* allele. This is a genetic test to help further our understanding of HIV-related dementia (memory loss and thinking problems) and other neurodegenerative disorders (neurodegeneration refers to the progressive loss of structure or function of nerve cells). Some versions of this allele may increase a person's risk of developing Alzheimer's disease in their lifetime. This *ApoE* test is for research purposes only and its result will not be reported to you or your physician.

8. MRI -- The MRI scanner is a powerful magnet that uses simple radio waves to take pictures of your brain. There is no pain associated with this procedure. You will be positioned on your back on the scanner bed and made to feel as comfortable as possible. The scanner bed will be moved inside a large tube so that your head and your chest are inside, but you will be able to see out into the room by your feet. During the scan, you will hear loud, rhythmic knocking sounds. Your ears will be covered to keep the noise at a minimum. There is a speaker and a microphone in the scanner so that you can talk to the MRI technician if there is something you need. Once the scan starts, you will need to lie still since moving around will interfere with taking pictures of your brain. You will be able to end the scan at any time if you feel uncomfortable. You may be asked to do a task while in the scanner. The MRI will take approximately 1 hour to complete. The images we acquire for this study are for specific research purposes and are not being used to evaluate your health or find medical abnormalities. These images will not regularly be reviewed by a radiology physician to diagnose existing abnormalities.

9. Sometime during your baseline assessments, you will be provided a stool collection kit to collect a stool sample to bring to your next visit. Preferably this sample will be from your first morning stool, but any stool sample not more than 24 hours old will be OK. When you bring in your sample, you will also be given a questionnaire to fill out about your recent diet.

We do not plan to analyze any human genetic material from these samples, but there will be some unique, individually identifiable genetic information that will be generated. All genetic sequences which we identify as human will be removed from the files before further analysis for metagenomic differences. Although it is unlikely, we may identify other genetic differences which predispose you to other conditions later in life. Some of these are currently known (i.e. Parkinson's disease), but other genetic differences which might predispose you to medical conditions like diabetes or hypertension, could be discovered in the future.

Of note, in order to minimize participants' potential exposure to COVID-19, any procedures that can be done remotely (such as neuropsychological assessments and questionnaires) will be done over the phone, via Zoom and/or Redcap whenever possible. When you're on campus, though, you will always be required to wear a mask.

INTERVENTION

Approximately 1-2 weeks after you complete all baseline testing, you will be randomly assigned to participate in one of two exercise programs. Both exercise programs will be done in group settings. Both programs will include a walk test every 20 sessions (approximately 5) to evaluate cardio endurance. One program will include things to build strength and increase your ability to supply oxygen to your body, such as lifting weights and walking fast or jogging on a treadmill. The other program will consist of mostly stretching to increase your flexibility and socialization. This means that the study treatment you receive will be determined purely by chance, like flipping a coin. You will have a 2 out of 3 chance of receiving the more strenuous of study treatments, but neither you nor the research team will know which study treatment you are receiving. We will, however, be able to access this information quickly if we need it to ensure your safety. You may be asked to wear heart-rate and blood pressure whenever you are in the gym, and if you have a history of diabetes, we may ask you to do one or more finger sticks at each session to monitor your sugar levels.

Once randomized, you will be scheduled to come in approximately 3 times per week for 26 weeks for a coached exercise session. While we hope you make every effort to come as scheduled, you will be able to make up missed visits in the weeks prior to or after your missed session. Your exercise training will be performed approximately three days/week under supervision by a member of the research team in our Exercise Training Facility (ETF). Depending on which group you are randomized to, your workouts might focus more on aerobic activities and resistance/strength training or stretching and flexibility. Either way, each session will start with a 5-min cycling warm-up on the stationary bicycle machine (or similar warm-up routine) followed by your planned exercise routine. All workouts to be performed will target all major muscle groups and will be adjusted to your abilities as you become stronger and more flexible. This will be followed by a 5-min cool-down period. At least once per month but possibly more frequently, your range of motion will be measured (SIS group only), as will the maximum amount of weight you can lift in one repetition (EXS group only). These measurements will be taken throughout the study to gauge your monthly progress.

You will be provided with a special face mask, face shield or goggles, gloves, and/or disposable gown (personal protective equipment, or PPE) to wear that will be required whenever you are in the gym.

One Month Stool Sample

Approximately one month into the intervention, you will be provided a stool collection kit to collect a stool sample to bring to your next visit. Preferably this sample will be from your first morning stool, but any stool sample not more than 24 hours old will be OK. When you bring in your sample, you will also be given a questionnaire to fill out about your recent diet.

Mid-Point Evaluation, Approximately Week 13

At approximately 3 months or approximately 39 visits into the intervention, you will be scheduled to complete a modified cognitive battery of memory tests and questionnaires. These are exercises that are related to memory, how fast you do things with your hands, and how you pay attention to tasks. There are a number of different tasks; some are timed and some are not. Questionnaires regarding your mood, ability to care for yourself, as well as your drug and alcohol history will be administered and you may skip any questions that make you feel uncomfortable. These will take approximately 1 hour to complete. There will be no MRI or labs completed at this visit, but you will be asked to provide another stool sample and complete a dietary survey as noted before at baseline and 1 month.

Post-Intervention follow up, Approximately Week 27

Approximately 1 week after you complete the exercise intervention, you will return to repeat the screening and baseline assessments you had before starting the intervention. These visits will be exactly the same as your initial ones, including the provision of a stool sample and dietary survey, except you will not have to complete the Locator Form again, unless your contact information has changed. We will remove the activity meter upon your return for the last follow-up appointment.

If you choose to drop out early or are withdrawn from the study before completion of the intervention, you may be invited to complete this post intervention follow-up at that time.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining blood, neuroimaging, neuropsychological, stool samples and laboratory data from you. We would like to use the stool, blood and data for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding HIV or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you. By allowing us to use the blood and data, you give up any property rights you may have the blood and data.

We will share your stool, blood and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We would like to also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

Your stool, blood and data will be stored without your name or any other kind of link that would enable us to identify which sample(s) or data are yours. Therefore, it will be available for use in future research studies indefinitely and cannot be removed.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 300 people will be enrolled in this study conducted by investigators at Washington University, with the expectation that approximately half will complete all assessments and interventions.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for:

- Screening visit = approximately 1 hour
- Baseline visit = approximately 4½-7 hours (2½ hours neuropsych and questionnaires plus 2 hours cardiorespiratory capacity testing and 1½ -2 hours for MRI and fasting labs). Depending on scheduling availability and your preference, these tests may be scheduled all on one day or split into separate visits.
- Intervention = approximately 1½-2 hours per session x 3 sessions per week x 26 weeks

- Mid-Point visit (approximately 3 months or approximately 39 visits) = approximately 1 hour. A modified neuropsych battery and questionnaires.
- Follow-up visit (approximately 2 weeks after intervention) = same as Baseline visit above

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. Some risks described in this consent document, if severe, may cause death.

RISK OF THE SCREENING, NEUROPSYCHOLOGICAL (MEMORY) TESTS, & QUESTIONNAIRES

Likely: None

Less Likely:

- You may feel embarrassed or uncomfortable answering some of the questions.
- You may experience fatigue or embarrassment from the exercises of memory, movement, and attention.

You may discuss any question that concerns you with the coordinator, and you may choose not to answer any question that makes you feel uncomfortable.

Rare: None

RISKS of MRI

You may be uncomfortable inside the MRI scanner if you do not like to be in closed spaces (“claustrophobia”). During the procedure, you will be able to talk with the MRI staff through a speaker system. You can tell them to stop the scan at any time.

The MRI scanner produces a loud hammering noise, which has caused hearing loss in a very small number of patients. You will be offered earplugs to reduce this risk.

There is a risk of burns that could be serious.

There is a risk of tissue heating which may cause you to feel very warm.

If you experience any of these symptoms and do not wish to continue, you can ask that the scan be stopped immediately.

Some things may interfere with Magnetic Resonance Imaging (MRI), and some can be potentially dangerous. You should inform the study doctor if you have any of the following:

- Heart problems
- Pacemaker
- Metal implanted under your skin, such as an insulin pump
- Hearing aid or cochlear implant
- Surgical clips or staples
- Any metal prosthesis. A prosthesis is an artificial body part, like an artificial leg.
- Shrapnel or bullet
- Tattooed eyeliner

- Metal dental items
- Braces
- Pregnancy

Devices

If you have a device such as a pacemaker, bone hardware, or device placed in your uterus there may be additional risks. We will review what device you have and inform you of these risks. In general, these risks could be:

- heating or movement of the device
- device malfunction
- damage to the tissue that surrounds the device.

Tattoos

If you have a skin tattoo, including cosmetic tattoos (eye-liner, lip-liner) you could experience the following:

- irritation, swelling or heating in the area of the tattoos
- in rare instances a primary or secondary burn.

If you have a tattoo we will offer you a cold, wet washcloth to put over the tattoo to reduce this risk.

Likely:

Metal in or on the body

The MRI scanner functions like a magnet and any metals in your body can be pulled off by the machine. If you have metal implants (under the skin) such as a pacemaker or metal pins or rods) you may be at risk when you are close to the machine. To minimize this risk, we will ask you a series of questions about metal exposure over the course of your lifetime from work experiences and medical procedures.

Claustrophobia (fear of small spaces)

When you have the MRI, you will lie on a small bed and the bed will be inserted inside a large tube. The opening of the tube is narrow, and some people can experience claustrophobia (anxiety or nervousness while inside small spaces) when in the scanner. If you believe that you may experience anxiety or nervousness while inside the scanner you should not participate in this study. If you decide to participate in the study and begin to experience claustrophobia while inside the scanner, we will immediately stop the procedure at your request.

Body Stiffness

You may also experience stiffness from lying still for a long time while in the scanner.

Less Likely: The scanner produces a loud repeating knocking noise during the scan that some people find bothersome. To lessen the noise, you may be given headphones.

Rare:

- Occasionally, some people may experience a short period of dizziness or feel faint after being in the scanner.
- There is a rare possibility that a serious abnormality may be discovered by the technician during the MRI picture of your brain. A radiologist will review MRI scans for clinical findings. If there is an incidental observation on the MRI which may be clinically significant, the Principal

Investigator (PI) will be contacted. If indicated, with your permission, the PI or his/her designee will contact your doctor with this information. If you request it, a copy of your brain MRI scan can be shared with your doctors. In this event, you will be referred to your primary care physician and/or the WUSM Neurology Clinic for clinical follow up and treatment as appropriate. While we will never put your consent form or study data in your medical records, once we notify your physician and make relevant brain MRI's and test results available to him/her for clinical follow up, that information may become part of your health care records.

RISKS ASSOCIATED WITH BLOOD DRAW, FINGER STICKS & INTRAVENOUS LINE

Likely: Pain, stinging, bruising and bleeding at the site of needle insertion.

Less Likely: None

Rare: Infection at the site or blood clot.

RISKS ASSOCIATED WITH CARDIORESPIRATORY CAPACITY TESTING

Exercise Stress Test (with Echocardiogram), Exercise Fitness Test (6-minute walk), Stationary Bike Test (VO₂ test)

Stress echocardiographic studies will be performed in the Cardiovascular Imaging and Clinical Research Core Laboratory, which is fully equipped with monitoring (blood pressure, 12-lead ECG, pulse oximetry) and emergency equipment (crash cart, intubation, and defibrillation equipment).

A physician is immediately available at all times.

Likely

- Shortness of breath,
- Fatigue

Less Likely

- Discomfort from pressure from the echo probe.
- Redness or skin irritation from the electrodes used for the EKG
- May fall off or injure yourself using equipment or during walk test; you could experience a break or a sprain.

Rare

- Increase in blood pressure
- Decrease in blood pressure
- Increase in heart rate
- Development of irregular heart rhythms
- Chest pain

Very Rare

- An abnormal heart rhythm could develop that would require treatment with an electrical shock and/or a heart attack may occur.
- Heart attack (estimate 9 per 10,000 tests or < 0.1%)
- Death (estimate 2 per 10,000 tests or <0.02%)

RISKS ASSOCIATED WITH DXA

Likely

Mild

This study will expose you to radiation from the DXA scan. The amount of radiation from this,

when averaged over your entire body, is 1/300 of the amount of radiation exposure all people in St. Louis receive each year from naturally occurring radiation sources. The risk from the radiation exposure in this study is too small to be measured. It is not a big risk when compared with other risks you take every day. If you want to know more about radiation exposure, please see the “Radiation Fact Sheet” located at <http://hrpo.wustl.edu> or ask the study staff for a copy.

Less Likely: None

Rare: None

You may not participate in this study if you are pregnant. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to research-related radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

RISKS ASSOCIATED WITH RANGE OF MOTION TESTING, EXERCISE & STRETCHING INTERVENTIONS

Likely

Mild

- Soreness or injury to tendons, ligaments, joints, and/or muscles

Less Likely: May fall off or injure yourself using equipment, you could experience a break or a sprain. Study staff will be in the room with you and monitoring you as you work out, however, there is always the possibility of an unforeseen accident. You may also experience some mild skin irritation from wearing the heart rate and blood pressure monitors, however, they can be adjusted to reduce your discomfort.

Rare

Serious

- Development of ventricular arrhythmia (rapid abnormal heart beat), myocardial infarction (a stop in the blood flow to your heart), cardiac arrest (a sudden stop in the circulation throughout your body because your heart stops working), and death. Although possible, we consider these events extremely unlikely. Repeated exercise testing of even high-risk patients (with known heart disease or with chronic kidney problems requiring dialysis) has been performed regularly in the Human Applied Physiology Laboratory for the past 27 years without any major complications. During the past 15 years, as part of ongoing research, we have performed maximal exercise tests on over 1100 people in the 65 to 96 year age range and performed multiple maximal exercise tests on more than 800 enrolled in our research projects without significant problems. In a large study of over 13,000 patients undergoing cardiac rehabilitation, the average complication rate was one non-fatal event for every 34,673 patient hours exercising, and one fatal event every 116,402 hours of exercise. Repeated exercise testing, when properly monitored under supervision of an experienced physician, does not appreciably increase the risk to the patient.

RISKS ASSOCIATED WITH WEARING PERSONAL PROTECTIVE EQUIPMENT (PPE)

Less Likely

- Feeling faint or lightheaded
- Feelings of breathlessness or suffocation
- Feelings of panic or panic attack

If you experience any of these feelings, you will be allowed to momentarily remove your mask while maintaining appropriate social distancing. Once these symptoms resolve, you will be asked to replace your PPE. If you are unable to unwilling to do so at that time, your study visit will be ended.

Rare

- Carbon dioxide (CO₂) toxicity, particularly in individuals with severe COPD or lung disease. Individuals with conditions that predispose them to CO₂ toxicity will likely not be eligible for the study, so the possibility of experiencing this risk is very rare.
- Changes in heart rate
- Irritated skin or possible infection due to build-up of moisture under the PPE

If you are a woman capable of becoming pregnant, we will ask you to have a pregnancy test before beginning this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to your unborn child, or risks to your unborn child that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to an unborn child. You must tell the doctor if your birth control method fails while you are on the study. If you believe or know you have become pregnant while participating in this research study, please contact the research team member identified at the top of this document as soon as possible. Please discuss with the research team how long you need to wait before becoming pregnant after completing the treatment or procedures on this study.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long term-care insurance.

We will use our best efforts to keep all information about you secure, and we think the risk of disclosure is small. Sequencing a large part of your genome does carry the risk that the resulting genetic data could one day be re-identified as your own. This can only happen with additional genetic data from you. One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because we anticipate that this study will provide valuable data to facilitate our understanding of the relationship between exercise and neurocognitive impairment in older HIV+ participants and may help future therapies

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you engage in an exercise regimen on your own

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any additional costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you, which may take up to 2-3 weeks before you receive it. If your social security number is obtained for payment purposes only, it will not be retained for research purposes. You will be compensated up to \$815 for participating in this study.

The total amount of compensation for being in the study will be up to \$815.00. Remuneration will be pro-rated based on how much of the study you complete:

- Screening and baseline assessments = \$175
 - Screening =\$5
 - Fasting Labs = \$10
 - Cardiorespiratory capacity testing = \$45
 - MRI = \$40
 - Neuropsych assessments = \$40
 - Questionnaires =\$10
 - Stool sample and dietary survey = \$25
- Intervention = \$390. Upon successful completion of each week of exercise @ 3x/week, you will be paid \$15. If you complete all 26 weeks, you receive \$390 (26 weeks x \$15/week). You may defer your weekly payment into fewer larger payments if you wish or be paid at the end of each week as noted above.
- 1-month stool sample and dietary survey = \$25
- Mid-Point assessments = \$25 + stool sample and dietary survey = \$25 (\$50 total)
- Follow-up +1 assessments = \$175
 - Screening =\$5
 - Fasting Labs = \$10
 - Cardiorespiratory capacity testing = \$45
 - MRI = \$40
 - Neuropsych assessments = \$40
 - Questionnaires =\$10
 - Stool sample and dietary survey = \$25

Payment will be made by either check or gift card, depending on availability.

Remuneration for the neuropsych assessments will be prorated, based on the per cent of assessments that you complete; for example, if you only complete half (50%) of the assessments, you will only receive half of the payment (\$20.00).

While in the study, transportation via bus/Metrolink tickets or taxi will also be provided for you if necessary.

If you complete the study, you will be provided with a 6-month membership to the BJC WellAware Center or other local gym, at the PI's discretion, in the hopes that you will continue your new-found exercise routine. If you choose to make use of this added benefit, we will continue to obtain data on how often you access the gym until your membership is complete.

WHO IS FUNDING THIS STUDY?

The National Institute of Health (NIH) is funding this research study. This means that Washington University is receiving payments from NIH to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NIH for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator (Dr. Beau Ances) at 314/747-8423 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University and NIH. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

WILL YOU KEEP MY NAME ON FILE TO GIVE TO OTHERS?

We will keep information about you in a special kind of computer listing called a registry. A registry keeps information about you on file so that *other* researchers, not involved in this particular study, may contact you in the future about whether you are interested in being in *different* research studies. The registry will contain information such as your name, address, age, and selected medical information such as diagnosis and treatment. We will keep the information in this registry secure by keeping it under two locks (for example, a locked file cabinet in a locked room). You may request that your personal information be removed from this file at any time by contacting the research team member identified at the top of this document.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

It is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- NIH
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be available to your health care providers who are not part of the research team.
- The last four digits of your social security number may be used in hospital or University systems

to track billing information for research procedures

- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Your primary care provider if a medical condition that needs urgent attention is discovered.

To help protect your confidentiality, we will keep all information in a locked area. The information you give us will be given a code number. A master list linking the code number and your identity will be kept separate from the research data. Only the Principal Investigator and people helping him will be able to see the list, and all staff involved with this project have been thoroughly trained in the protection of research participants. We will protect your information, but there is a chance somebody might see it. We will protect your genetic information by using a code which cannot be traced back to you. This code will be assigned once we've collected all of the information we need for our study from your medical record. This may take up to one month. We will not sequence your DNA until your identifiers have been stripped.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

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.

To further protect your privacy, the investigator has obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate may prevent the investigator from being forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the investigator from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you request in writing that information about you or your participation in the research be released to an insurance company, the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own privacy. Finally, the investigator is not prevented from disclosing, including reporting to appropriate authorities, information concerning abuse, neglect or harm to others or yourself.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
- To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at <https://hrpo.wustl.edu/participants/withdrawing-from-a-study/> or you may request that the investigator send you a copy of the letter.
 - **If you revoke your authorization:**
 - The research team may only use and share information already collected for the study.
 - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
 - You will not be allowed to continue to participate in the study.

Can we contact you by email?

We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you, such as

- appointment scheduling/reminders containing PHI
- copies of current/updated consent forms and other information for this study
- consent forms and information for other studies you have requested.

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an

urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer, you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

Do you agree to allow us to send your health information via email?

_____ Yes _____ No
Initials Initials

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at <https://hrpo.wustl.edu/participants/withdrawing-from-a-study/> under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason; because you have certain medical conditions like seizures, use of illegal drugs, or pregnancy; because in our judgment it would not be safe for you to continue; or because the funding for the research study has ended.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please

contact Elizabeth Westerhaus at 314/747-1125 or Dr. Beau Ances at 314/747-8423. If you experience a research-related injury, please contact: Elizabeth Westerhaus at 314/747-1125 or Dr. Beau Ances at 314/747-8423.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, <http://hrpo.wustl.edu>. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 07/16/19.

(Signature of Participant)

(Date)

(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

(Signature of Person who Obtained Consent)

(Date)

(Name of Person who Obtained Consent - printed)