Title: High-Intensity Interval Training to Improve Symptoms of Deployment-Related Respiratory Disease

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Subject Name: _____ **Date:** _____

Title of Study: High-Intensity Interval Training to Improve Symptoms of Deployment-Related Respiratory Disease – A Pilot Study

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Key Information

You are being asked to be in a research study. Participation in the research study is voluntary. The purpose of this study is to learn more about exercise problems in military personnel who have been exposed to airborne hazards due to deployment. The expected duration of your participation is 4 months. The research procedures will include exercise testing, breathing tests, exercise echocardiogram (heart ultrasound), and exercise training. The main risks are discomfort related to exercise or testing procedures. The main anticipated benefits are increased fitness and increasing knowledge about deployment-related exercise problems. If you choose not to participate in this study, you may continue with your regular healthcare as suggested by your medical team.

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?

This study plans to learn more about exercise intolerance in military personnel who have been exposed to airborne hazards (burn pit combustion products, dust, sandstorms, etc.) due to deployment. It will investigate cardiac (heart) and pulmonary vascular (lung blood vessel) abnormalities that may contribute to exercise tolerance. Additionally, the study will test whether high-intensity interval training (HIIT) improves symptoms in individuals with respiratory symptoms after airborne hazards exposure.

You are being asked to be in this research study because you may have had airborne hazards exposure through your deployment and you are experiencing symptoms with exercise.

Other people in this study

Up to 36 people from your area will participate in the study.

What happens if I join this study?

If you join the study, you will complete up to four research visits (Visits 1A, 1B, 2A and 2B) and up to 12 weeks of high-intensity interval training.

- Visit 1A will occur first and will include the following tests: maximal exercise test on a bicycle, spirometry (breathing tests), questionnaires, radial arterial catheter placement, IV insertion, and blood draws. The arterial catheter is similar to an IV but is placed in the radial artery in your wrist rather than a vein in your arm. It will be used for blood pressure monitoring and arterial blood draws. The arterial catheter will be left in place while you exercise and removed at the end of the exercise test. The IV will be left in place while you exercise and removed at the end of the exercise test. Blood draws will be performed through the IV and arterial line that are placed. Small amounts of blood will be drawn throughout the exercise test, totaling approximately 2-3 tablespoons of blood. A participant may skip any questions on the questionnaires that he/she prefers not to answer. Visit 1A will take approximately 1.5 hours.

- Optional Visit 1B will occur next. If you and the study team determine that you will do Visit 1B, it will include an echocardiogram (ultrasound of your heart) before and after exercise. You may be asked to complete a COVID-19 rapid antigen test (nasal swab) at the beginning of the visit. The total amount of exercise will be ~10 minutes and the entire visit will take approximately 1.5 hours.

- After Visit 1A and Optional Visit 1B, you will be asked to complete the exercise intervention. It includes up to 12 weeks of 3x/week high-intensity interval training (HIIT). Each HIIT session will include up to ~40 minutes of exercise on a stationary bicycle. Additionally, you will be asked to complete 3x/week of up to 40-minute sessions of moderate aerobic exercise.

- After completing the exercise intervention, you will return for Visit 2A and Optional Visit 2B which will include the same tests as Visits 1A and 1B. Visit 2A will take approximately 1 hour and Visit 2B will take approximately 1.5 hours.

Visits 1A, 1B, 2A and 2B and HIIT sessions will take place at the University of Colorado Anschutz Medical Campus. You will complete the aerobic exercise sessions at home or anywhere else where you might exercise.

This research study is expected to take approximately 1 year. Your individual participation in the project will take 4 months.

Due to physiologic changes of pregnancy which may impact the response to exercise training, pregnant women or women who anticipate becoming pregnant during the course of the study are not eligible to participate. A urine pregnancy test will be performed during Visit 1A.

What are the possible discomforts or risks?

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

Discomforts you may experience while in this study include those related to vigorous exercise, including fatigue, shortness of breath, leg discomfort, lightheadedness and muscle or joint pain.

Other possible risks include pain or bleeding at the site of radial artery catheter insertion and peripheral intravenous catheter insertion (Visits 1A and 2A), abnormal heart rhythm, and heart attack. We will use standard practices including lidocaine and ultrasound guidance to minimize the risks of radial artery catheter placement. Risks of spirometry (breathing tests) include mild discomfort or lightheadedness related to deep breathing. Risk of COVID-19 rapid antigen test include nasal discomfort. During maximal exercise tests and HIIT sessions you will be monitored by trained research personnel and exercise will be stopped immediately for any concerning signs or symptoms. If at any time during the study we identify any unique risks to you starting / continuing an exercise program, we will tell you about those risks and remove you from the study.

There is a risk that people outside of the research team will see your research information. We will do all we can to protect your information, but it cannot be guaranteed.

There is a risk of loss of confidentiality. Study visits take place in the University of Colorado Clinical and Translational Research Center (CTRC). The CTRC is staffed by medical personnel who have been educated on the importance of privacy, confidentiality and protected health information. Protected health information will not be discussed or disclosed in non-private settings. However, by attending study visits there is a risk of loss of confidentiality.

The study may include risks that are unknown at this time.

Risks of the usual care you receive are not risks of the research and are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

If you become pregnant, the procedures involved in the study may involve risks to the embryo or fetus which are currently unclear. You should not participate in this study if you anticipate becoming pregnant during the study. We will ask you to complete a pregnancy test at Visit 1A.

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

What are the possible benefits of the study?

This study is designed for the researcher to learn more about exercise intolerance after airborne hazards exposure. You will be provided with your test results as well as supervised exercise (HIIT) training.

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.

Are there alternative treatments?

There may be other ways of treating your exercise symptoms. These other ways include other forms of exercise training or medications like inhalers. You could also choose to get no treatment at all.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

This research is being supported by the Department of Veterans Affairs Airborne Hazards and Burn Pits Center of Excellence Pilot Project Program and the National Institute of Health through funding to the Colorado Clinical and Translational Sciences Institute Clinical and Translational Research Center (UM1TR004399).

Will I be paid for being in the study?

You will be paid $50 for each of Visits 1A, 1B, 2A and 2B and $400 for the exercise program. The total amount possible to be paid to you is $600 if you complete Visits 1A, 1B, 2A, 2B and the exercise program visits. You will be paid this sum at the completion of the study. If you leave the study early or if we have to take you out of the study, you will be paid at that time the prorated sum for the study visits (including exercise program visits) you have completed.

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

Your SSN will be collected and used to report this taxable income to the IRS.

The VA is not required to provide treatment for injuries in research studies if the injuries are caused by your non-compliance with study procedures.

You should inform your care provider(s) if you decide to participate in this research study. If you have questions about an injury related to the research, call the study PI (Dr. Lindsay Forbes) at [redacted] or VA PI (Dr. Silpa Krefft) at [redacted].

If you have an injury while you are in this study, you should call the study PI (Dr. Lindsay Forbes) or VA PI (Dr. Silpa Krefft) immediately. You may reach them by calling [redacted] or [redacted]. Emergency and ongoing medical treatment will be provided as needed.

Who do I call if I have questions?

The researcher carrying out this study at the VA is Dr. Lindsay Forbes and Dr. Silpa Krefft.

You may ask any questions you have now. If you have any questions, concerns, or complaints later you may call Dr. Lindsay Forbes at [redacted] or Dr. Silpa Krefft at [redacted]. You will be given a copy of this form to keep.

If you have questions regarding your rights as a research subject, concerns or complaints about this research study, please call the Colorado Multiple Institutional Review Board (COMIRB) office at 303-724-1055. This is the Board that is responsible for overseeing the safety of human participants in this study. If you want to verify that this study is approved or if you would like to obtain information or offer input, please contact the VA Research Office at 720-857-5092

Will I be told new information about this study?

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.

Who could profit from the study results?

The study results are not intended to be used for commercial profit. However, if a commercial product is developed based on the results of this study in the future, you will not receive compensation for such a product.

How will my private information be protected?

Taking part in this study will involve collecting private information about you. We may ask for the final four digits of your social security number in order to access your medical records. You may choose to withhold your social security number and still participate, so long as we can use an alternative identifier like your birthdate to access your medical records. We will only access medical records that are relevant to your participation in this research study. We will keep all research records that contain your identifiable health information confidential to the extent allowed by law. Records about you will be kept on computers protected with passwords to which only the study team will have access.

Identifiers might be removed from the identifiable private information, data, or identifiable biospecimens that are collected. After that removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

A description of this clinical trial will be available on http: http://www.clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who will see my research information?

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

- Federal agencies such as the Food and Drug Administration (FDA), the General Accountability Office (GAO), the Office of the Inspector General, Office for Human Research Protections (OHRP), and the Office of Research Oversight (ORO) that protect research subjects like you, may also copy portions of records about you.
- People at the Colorado Multiple Institution Review Board
- The investigator and research team for this study
- The sponsor Department of Veterans Affairs Airborne Hazards and Burn Pits Center of Excellence (AHBPCE) (group paying for the study), study monitors, or agents for the sponsor
- Officials at the institution where the research is being conducted, and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research
- Our local VA Research and Development Committee
- University of Colorado – Colorado Clinical and Translational Sciences Institute Clinical and Translational Research Center
- University of Colorado School of Medicine Metabolomics Core
- University of Colorado Clinical Research Support Team
- UCDenver and its Clinical Trials Management Systems

I understand that by signing this consent form, a copy of limited data about me, restricted to all research data that is collected as part of this specific VA research study, will be stored in the REDCap database (or Data Storage System) at the University of Colorado Denver's (UCD's) Colorado Clinical and Translational Sciences Institute (CCTSI). This data will be used solely for the purposes defined in this consent form and for this specific study. Data collected about me for this study placed on the CCTSI REDCap Database will not be accessed or used for any other study or purposes, and will only be accessed by the study team. The CCTSI REDCap Database is a highly secure, nationally-utilized data management system, and it is housed within the highly-secure environment at the University of Colorado Denver.

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

We will ask you to sign a different form that talks about who can see your research records. That form is called a HIPAA Authorization form. It will mention companies and universities who will see your research records.

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

The HIPAA Authorization form that you will also be asked to sign will state when or if it expires. However, you may withdraw this authorization for use and disclosure of your personal health

information by providing written request to the Investigator. If you withdraw the HIPAA Authorization form, the Institution, the Investigator, the research staff, and the research Sponsor will no longer be able to use or disclose your personal health information from this study, except so far as that they have already relied on this information to conduct the study.

Is there other information I need to know?
You will be provided with a summary of your personal study results at the conclusion of your participation in the study. Additionally, you will receive a report of the overall study results once the study is complete.

Agreement to be in this study

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

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

Subject's Signature: _____ Date:_____

Print name: _____

Consent form explained by: _____ Date: _____

Print name: _____

OPTIONAL ADDITIONAL PROCEDURES

Optional Consent for Data and Specimen Banking for Future Research

Dr. Lindsay Forbes would like to keep some of the data and blood 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 deployment-related respiratory disease and/or exercise training. The research that is done with your data and samples is not designed to specifically help you. It might help people who have deployment-related respiratory disease 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. Lindsay Forbes 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 Dr. Lindsay Forbes 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. Lindsay Forbes decides to destroy them.

Your data and samples will be able to be accessed only by Dr. Lindsay Forbes and the study team. If your data and samples are given to other researchers in the future, Dr. Lindsay Forbes will not give them your name, address, phone number or any other information that will let the researchers know who you are.

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.'

Federal laws and policies provide you with protection from discrimination by health insurance companies, group health plans, and most employers based on your genetic information. A federal law called the Genetic Information Nondiscrimination Act (GINA) generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information obtained from this study.

- Health insurance companies and group health plans may not use your genetic information obtained from this study when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information obtained from this study when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. It also does not prohibit discrimination on the basis of already known genetic disease.

The possible benefits of research from your data and samples include learning more about what causes deployment-related respiratory disease 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. Lindsay Forbes 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. Lindsay Forbes.

Please read each sentence below and think about your choice. After reading each sentence, check "yes" or "no" and initial. If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data and blood to be stored in a central tissue bank at University of Colorado for future use by the study investigators:

1. I give my permissions for my data and blood to be kept by Dr. Lindsay Forbes for use in future research to learn more about how to prevent, detect, or treat deployment-related respiratory disease.

   ☐ Yes ☐ No _____Initials

2. I give my permissions for my data and blood 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 from either within the VA or outside of the VA in the future to ask me to take part in more research.

   ☐ Yes ☐ No _____Initials