Dr Hayley Scott
Priority Research Centre for Healthy Lungs
Level 2 West Wing, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
T: 02 4042 0113
Fax: 02 4042 0046

Participant Information and Consent Form

The Impact of Varying Exercise Training Intensity on Clinical Asthma Outcomes and Inflammation in Adults with Asthma

Invitation
You are invited to participate in a research study examining how three months of exercise training affects asthma symptoms and inflammation in the airways of adults with asthma. This study is being conducted by Dr Hayley Scott, Prof Lisa Wood and Prof Robin Callister from The University of Newcastle and Hunter Medical Research Institute, and Prof John Upham from The University of Queensland.

Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of the research team will also explain the study to you. If you do not understand any of the information or have any worries, please ask us.

What is the purpose of this study?
It is well known that exercise has numerous health benefits; however, the effects of exercise on asthma symptoms and inflammation in the lungs is not clear. Previous research suggests that exercise may improve asthma and reduce inflammation in the lungs of those with asthma, but more research is needed.

This research therefore aims to improve our understanding of the role of exercise in those with asthma. We hope to find new ways to manage asthma and to allow for the development of improved management guidelines for health professionals. We seek to compare exercise training at different intensities to find out if they have different effects on asthma.

Why have I been invited to participate in this study?
This study may be suitable for you because you have a confirmed diagnosis of asthma and are aged 18-55 years old. If you are a current smoker, undertaking exercise training (more than 90 minutes a week), have a heart condition or diabetes, taking cholesterol lowering medication, are pregnant or breastfeeding, or have a body mass index (BMI) ≥40kg/m^2 (or BMI ≥30kg/m^2 if you are a male aged 46-55) then this study may not be suitable for you.

What if I don't want to take part in this study, or if I want to withdraw later?
Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

If you decide to withdraw from the study, you have the option of withdrawing all data relating to you and have any samples that have been taken destroyed. An exception to this is in the case of an adverse event, or a serious adverse event, where the data needs to be retained for regulatory reporting.

The researchers may withdraw a participant if it is considered in the participant's best interest or it is appropriate to do so for another reason. If this happens, the researchers will explain why and advise you about any follow-up procedures or alternative arrangements as appropriate.

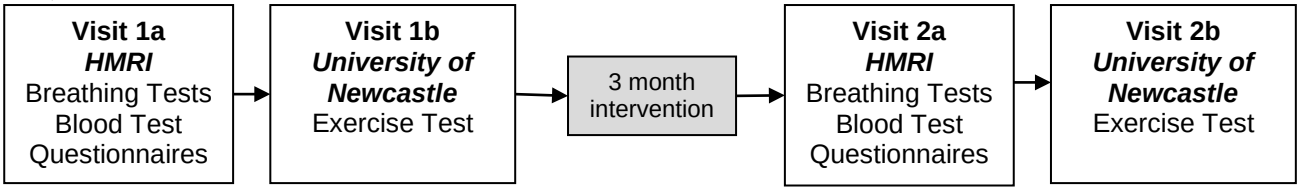
What does this study involve?
If you agree to participate in this study you will be asked to sign the Participant Consent Form. We will also need to check that the study is suitable for you and to do this we will invite you to come into the research facility at Hunter Medical Research Institute (HMRI) for a screening visit, which will take approximately 1 hour. During this visit the tests you will perform include:

- A brief medical examination including measurement of your height, weight and blood pressure;
- Some breathing tests, which involves you breathing into some tubing. This will allow us to measure your lung function and assess if there is any inflammation in your airways.

If this study is not suitable for you, we will advise you of the results and, with your permission, will forward this information to your GP for follow up. If this study is suitable, we will organise a mutually convenient time for you to begin the study.

If you choose to participate, you will be randomised (like tossing a coin) to one of the three study arms: (i) moderate-intensity exercise training, (ii) vigorous-intensity exercise training, or (iii) control condition (no intervention). You will have an equal chance of allocation to each group but we cannot place you in the group of your choice. This study lasts for three months and involves two visits to the Hunter Medical Research Institute and two visits to The University of Newcastle exercise lab, Callaghan campus for assessments. If you are randomised to one of the exercise groups you will also attend The University of Newcastle exercise lab three times each week (one hour/session), for three months, where you will complete an exercise training program where you will be trained by an exercise physiology student.

Study Visit Schedule



Clinic visits:
Visit 1a and Visit 2a (HMRI): These visits will take approximately 3 hours each. Prior to coming to HMRI, you will need to withhold your asthma medications for 6-24 hours, depending on which medications you use, and antihistamine medication for 5 days. However, if you feel that your symptoms worsen significantly during this time, you should use your normal medications and then come to the clinic as planned. We would also like you to fast for 12 hours prior to your scheduled visit, however you may continue to drink plain water.

- **Breathing tests** – Your lung function will be measured by blowing into a spirometer, a machine that measures the amount of air expelled from your lungs. You will be asked to blow into the spirometer until your lungs are empty (approximately 6 seconds). We will also measure your exhaled nitric oxide, which will require you to breathe out gently into some tubing for 10 seconds. These are routine breathing tests with no known adverse effects,

except for perhaps some breathlessness and/or dizziness which usually lasts for a few seconds only.

- **Saline Challenge** – You will be asked to inhale a mist of salty water delivered by a nebuliser for 30 seconds, 1 minute, 2 minutes, and three lots of 4 minutes. A breathing test will be done at the end of each period and you will be asked to produce a specimen of sputum. This is a routine clinical test that we perform to measure the amount of inflammation in your airways. This test will be stopped at your request or if you develop any problems with your breathing, at which time you will be given a reliever medication (Ventolin). We will closely monitor your symptoms and breathing throughout the test. The sputum sample collected will be used to look at the amount of inflammation in your airways.

- **Blood Test** – Approximately 20mL (4 teaspoons) of blood will be taken from a vein in your forearm, to measure levels of inflammation and antioxidants in your blood.

- **Body Composition** – Your height, weight and waist circumference will be measured. We will also measure your body composition and bone density using a dual energy x-ray absorptiometry (DXA) machine. This is a very low dose form of x-ray, which is used to study body composition and bone strength. In particular, we can look at body fat and muscle distribution. It is not painful and takes approximately 20 minutes to perform the test. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. A DXA scan delivers <0.010 mSv. At this dose, no harmful effects of radiation have been demonstrated and the risk is negligible. The dose of radiation from this test is similar to the dose of naturally occurring background radiation that everyone is exposed to in two days. All radiation exposures will be carried out in accordance with the ARPANSA Code of Practice “Exposure of Humans to Ionizing Radiation for Research Purposes” (RPS8)”.

- **Blood Pressure and Oxygen Saturation** – Your blood pressure will be measured using an automatic blood pressure monitor. Your oxygen levels will be measured using a machine called an oximeter, which clips onto your finger.

- **Questionnaires** – We will ask you to wear an accelerometer on your wrist like a watch or around your waist on a strap for one week before each visit, to record your activity levels. We will also ask you to complete a food diary for four days before each visit. During the visits, you will be asked to complete questionnaires related to your asthma, quality of life, exercise habits and perceptions of exercise before and after the program. There will be an additional questionnaire for women only asking about your menstrual history. These questionnaires will take approximately 40 minutes to complete. Throughout the 3 month study period, we will also ask you to complete a short online questionnaire each week about your asthma symptoms and exercise levels. This will take only a few minutes to complete.

- **Allergy skin prick test** – Small amounts of fluid, each containing a common allergen (grass, dust mite, mould, cat hair, dog hair), will be put on your skin and then tiny pricks will be made on the skin at this location (this doesn’t break the skin and is not painful). We will test a panel of common environmental allergens to find out if you are allergic. If you are allergic to the fluid, a small itchy lump that looks like a mosquito bite will occur. The itchiness only lasts for fifteen minutes or so and if it is annoying we can give you some cream, which will take the itch away.

Visit 1b and Visit 2b (Exercise Laboratory, The University of Newcastle):

- **VO_2max Exercise Test** – You will perform a progressive exercise test on either a treadmill or exercise cycle ergometer. The test commences at an easy workload and becomes progressively harder every 30 seconds until you voluntarily end the test or you reach pre-

determined end criteria. Throughout the test, we will continuously monitor your heart rate using a heart rate monitor held in place with a strap around your chest. We will also measure oxygen usage and ventilation. In order to measure these, you will wear a face mask and the air you breathe out will be sampled for analysis. You can end the test at any stage. This test will measure your fitness level.

Exercise Programs:

The exercise training programs will involve aerobic exercise training where you will use exercise machines (treadmill, stepper, cycle), with all your training being fully supervised by an exercise physiology student. During this time we will get you to complete a weekly online asthma symptom and exercise questionnaire and wear a pedometer.

(i) Vigorous-Intensity Exercise Training Group

For this intervention, you will complete three supervised training sessions each week for three months at The University of Newcastle Exercise Lab. Each workout will run for one hour and will include a warm-up and cool-down. You will be asked to exercise at an intensity that would be perceived as "hard". Your workout will be based around your own level of fitness, where you will be exercising at a similar level as if you were playing soccer or jogging. Your heart rate will be monitored by your trainer throughout your workouts to ensure your safety and wellbeing, while also ensuring you are exercising at the desired level. The heart rate monitor will be held in place with a strap around your chest.

(ii) Moderate-Intensity Exercise Training Group

For this intervention, you will complete three supervised training sessions each week for three months at The University of Newcastle Exercise Lab. Each workout will run for one hour and will include a warm-up and cool-down. You will be asked to exercise at an intensity that would be perceived as "somewhat hard". Your workout will be based around your own level of fitness, where you will be exercising at a similar level as if you were walking briskly, dancing or playing doubles tennis. Your heart rate will be monitored by your trainer throughout your workouts to ensure your safety and wellbeing, while also ensuring you are exercising at the desired level. The heart rate monitor will be held in place with a strap around your chest.

(iii) Control Group

If you are randomised into this group, you will receive no active intervention; however, we would like you to return to the clinic after the three-month intervention period to complete Visits 2a and 2b. These visits have been described in detail above. This will enable us to draw conclusions about the effectiveness of the exercise training interventions.

Are there benefits or risks to me in taking part in this study?

Your participation in this study will benefit our understanding of asthma but you may not benefit personally from the study. All information about your condition will be available to you. If the study is suitable for you and you agree to participate you have a two in three chance of receiving three months of exercise training at The University of Newcastle free of charge. If you are randomised to the control group you will receive an activity pedometer at your final visit for you to keep. All car parking throughout the study will be free of charge.

The exercise sessions may make you breathless or cause a temporary worsening of your lung condition, in which case you will be given time to rest and recover. Although unlikely, you may experience some chest tightness or chest pain and if this occurs you should notify your trainer immediately. Your heart rate, oxygen levels and symptoms will be monitored throughout the test and if an unusual response is observed or you experience chest pain or excessive breathlessness, the test will be terminated and you will be monitored until recovery. Your heart rate, oxygen levels and blood pressure will be monitored until they return to normal after completion of exercise. The research team will pre-medicate you with salbutamol (Ventolin) prior to the exercise test and you

will also be advised to take your medication prior to each training session. This will help keep your airways open and minimise the risk of breathlessness during exercise. You may also experience some minor soreness in your leg muscles, particularly the day after the exercise sessions. The side effects of having blood collected may include bleeding or bruising at the injection site and possible dizziness and/or fainting. Please advise the research team if you normally feel dizzy or faint when you have blood collected. The saline challenge test can cause difficulty breathing, coughing, wheezing and some discomfort in your chest. This is not a sign of heart problems but is usually due to a slight tightening of the air passages in your lungs. This is brief and responds promptly to reliever medication (Ventolin, salbutamol). If you are allergic to one of the allergens applied in the skin prick test you may find you have an itchy lump on your skin. We can give you some cream to help relieve the itchy lump, with the itchiness usually only lasting for about 15 minutes.

What happens if I suffer injury or complications as a result of the study?
If you suffer any injuries or complications as a result of this study you should contact the study coordinator as soon as possible, who will assist you in arranging appropriate medical treatment.

How will my confidentiality be protected?
Of the people treating you, only the researchers named below and other clinical staff involved in your care will know whether or not you are participating in this study. Any identifiable information that is collected about you in connection with this study will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named below will have access to your details and results that will be held securely in the Centre for Healthy Lungs, The University of Newcastle.

What happens with the results?
Your participation in the study will benefit our understanding of respiratory disease management. All information about your condition will be available to be sent to your general practitioner at your request. The results of the study will also be available to you at the completion of the study; however you should be aware that the study may take over a year to complete.

We plan to discuss/publish the results of the study. We may also use the stored data in future trials, for which ethical approval will be sought prior to commencement. In any publication, information will be provided in such a way that you cannot be identified.

For all participants in the study we would like to access and record the visits and lung function results in your medical records. This will involve our staff accessing your medical record and recording the results of your visit in your patient notes.

What should I do if I want to discuss this study further before I decide?
When you have read this information, one of the named researchers will discuss it and any queries you may have with you. If you would like to know more at any stage, please do not hesitate to contact any of the investigators on the numbers listed.

Dr Hayley Scott
Postdoctoral Research Fellow
Centre for Healthy Lungs
Level 2, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
Tel: 02 4042 0113
E: hayley.scott@newcastle.edu.au

Prof John Upham
Senior Respiratory Physician
Lung and Allergy Research Centre,
Level 5, Translational Research Institute
37 Kent Street,
Woolloongabba QLD 4102
Tel: 07 3443 8024
E: j.upham@uq.edu.au

Prof Lisa Wood
Professor of Nutritional Biochemistry
Centre for Healthy Lungs
Level 2, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
Tel: 02 4042 0147
E: lisa.wood@newcastle.edu.au

Prof Robin Callister
Professor of Exercise Physiology
Centre for Physical Activity and Nutrition
Level 3 ATC Building, The University of Newcastle
University Drive,
Callaghan NSW 2308
Tel: 02 4921 5650
E: robin.callister@newcastle.edu.au

Ms Sarah Valkenborghs
PhD Candidate and Research Assistant
Centre for Physical Activity and Nutrition
Level 3 ATC Building, The University of Newcastle
University Drive,
Callaghan NSW 2308
Tel: 02 4042 0819
E: sarah.valkenborghs@newcastle.edu.au

A/Prof Chris Grainge
Consultant Respiratory Physician
Centre for Healthy Lungs
Level 2, HMRI Building
Lot 1 Kookaburra Circuit,
New Lambton Heights NSW 2305
Tel: 02 4921 3542
E: christopher.grainge@hnehealth.nsw.gov.au

Who should I contact if I have concerns about the conduct of this study?

This protocol has been reviewed and approved by the Hunter New England Research Ethics Committee (Reference Number 17/04/12/4.03). Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to Dr Nicole Gerrand, Professional Officer, Hunter New England Human Research Ethics Committee, Hunter Health, Locked Bag 1, New Lambton NSW 2305, telephone (02) 49214950, email Nicole.Gerrand@hnehealth.nsw.gov.au.

Thank you for taking the time to consider this study.
If you wish to take part in it, please sign the attached consent form.
This information sheet is for you to keep.

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Participant Consent Form

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I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the information statement, a copy of which I have retained.

I understand I can withdraw from the project at any time and do not have to give any reason for withdrawing.

I consent to-

- ☐ Completing the tests involved in the study
- ☐ Completing questionnaires to obtain research data
- ☐ A copy of my results being sent to my General Practitioner
- ☐ Allowing research personnel access to my medical record and to record attendance and results in my file
- ☐ Having my blood/sputum samples stored for use in future research. If I decline to have samples stored, I am still able to participate in the study

I have had the opportunity to have questions answered to my satisfaction.

Name _____

Signature _____ **Date** _____

I have informed the above person about this research and am sure that they understand both the content of the Information statement and the additional information I have provided.

_____
Investigator/Delegate Name (printed)