Participant Information Sheet

A Study to Compare Effects of Interval Training (HIIT) plus High Flow Nasal Oxygen (HFNO) versus HIIT plus traditional oxygen in Patients with Interstitial Lung Disease (ILD).

You are being invited to take part in our research study. Before you decide if you would like to take part, it is important for you to understand, why this research is being done and what it involves. Please take your time to read this information sheet carefully. A member of our research team will also go through this information sheet with you when you attend assessment for this study and will answer any questions you have regarding participation. You may also discuss with you general practitioner if you wish.

1. What is the background and purpose of this study?

We know that patients who suffer from Interstitial Lung Disease (ILD) better known as Pulmonary Fibrosis decline their levels of oxygen in the blood when they do physical activity, leading to reduced ability to carry out the daily activities. Pulmonary rehabilitation is a treatment for patients with ILD but fall in oxygen levels is a barrier to achieve good results from this treatment. For this reason, we want to evaluate if interval training (HIIT), which divides the training into high-intensity exercise by resting periods plus High Flow Nasal Oxygen (HFNO), which is a new modality to deliver oxygen and that can deliver high flows of oxygen improves the exercise capacity, which will be assessed with an exercise test on a bicycle. We believe that this type of training in combination with high flows of oxygen might reduce the fall of oxygen in the blood and consequently to improve the exercise tolerance.

This may constitute an alternative during pulmonary rehabilitation that may lead to better results of the treatment.

2. Why have I been invited?

You have been invited to participate in this study because you have been diagnosed with ILD. This study will involve 30 participants approximately.

3. Do I have to take part?

No, it is completely up to you to decide if you would like to take part or not. We will go through this information sheet with you again at your pre-study assessment. If you wish to participate, you will be asked to sign an Informed Consent Form. Your general practitioner will also be informed of your participation if you agree. However, you are free to change your mind at any time during the study without giving a reason. If you decide not to participate, your usual medical treatment and care will not be affected in any way, or your legal rights.

4. What will happen to me if I take part?

If you decide to participate in this study, you will be asked to read carefully and sign the Informed Consent Form. A copy of the signed form will be given to you to take away for your own records.

Our study will consist of 8 weeks of intervention plus 1 day of evaluations before and after the intervention (See flowchart 1). Considering that intervention will be 3 times per week for 8 weeks, you will need to visit the hospital a total of 26 times. All the visits will take place in ward 204 (Respiratory Medicine) of the Royal Infirmary of Edinburgh (for participants from Edinburgh) and in the Royal Victoria Infirmary (for participants from Newcastle).

The following measurements will be conducted:

Baseline Visit: we will take a blood test around 6mls (around a tablespoon) to know the levels of biological molecules found in the blood associated with fibrosis that have been shown to be related with disease progression. After this, we will perform a test called the quadriceps maximal voluntary contraction test (QMVCT). This will measure the strength of your thigh muscle (Quadriceps). You will be seated in a chair, with hip and knee bent to 90 degrees.

A strap is placed around your ankle, to ensure the knee remains at 90 degrees. The ankle strap is connected to a strain gauge mounted on the back of the chair. A seatbelt will be fastened over your hips to stabilise your pelvis. You will then do a knee extension so we can measure the strength of your thigh muscle .

After this test, we will assess how short of breath you feel using a scale from 1 to 5.

During this visit, we will measure your height and weight. Breathing tests will not be performed, because these procedures you have already done in the outpatient clinic. We will take the results of your tests from the clinic.

At this visit we will also ask you to carry out a maximal exercise test on a bicycle called Cardiopulmonary Exercise Test (CPET) (see figure 1). We will get you on the bicycle first, after 1 minute we will start you exercising with a warm up period of 3 minutes easy pedalling. After this, we start increasing the workload as though you were going up a hill. We want you to really push yourself and do as much as possible. The workload progressively increases, and the test is completed when you are too breathless to continue. The purpose of this test is to measure how long your lungs and heart are able to do exercise.

Once you have recovered from the bit above. Also, on the bike we would like to be able to measure how long you are able to exercise for. To do this the workload will be constant, (this will be 75% of what you managed to achieve during the previous test) and you will cycle until you feel that you need to stop. If you want to stop the procedure at any time, then you can.

The test typically lasts up to an hour but you will be exercising for no more than 15 minutes, during which you will need to exercise to the best of your ability. When you have completed the exercise, you will be monitored whilst you rest and your body recovers.

You will be able to rest for about 20 minutes between each test and we will offer you refreshments.

Therefore, we can monitor you; we will ask you to apply stickers (called electrodes) and a band to your chest to monitor your heart rate and rhythm. Some men may need to have a small area of their chest shaved in order for the electrodes to stick to the skin, we can help with this. We will also check your blood pressure during the test. We will also monitor your oxygen levels by a small clip on your finger.

Physical activity levels in daily life will also be measured using Actigraph GT3x activity monitor, which will be given to you during your baseline appointment to use in your house for only 1 week before and 1 week after of the intervention, this is a belt that you will have to use like any other. If something happens to the belt, we will give you a new one and you do not have to pay for anything. After of the intervention you should return it to us during your post intervention appointment.

We would also like you to answer two questionnaires called St George's Respiratory Questionnaire (SGRQ) and the Hospital Anxiety and Depression Scale (HADS), to measure your quality of life and anxiety and depression levels. The questionnaires you can answer them in the clinic while you are resting after your first bicycle test during the first day of the intervention and during your post intervention appointment.

Intervention, a group of participants will be submitted to 8 weeks of a PR program based on interval training (HIIT) on a bicycle plus high flow nasal oxygen HFNO and the other group will also be submitted to 8 weeks of a PR program based on HIIT but with conventional oxygen delivery without HFNO. Both trainings will be performed at the same workload, which will be progressive throughout the 8 weeks and will be modified during each session. Take into account that both groups will do the same, the unique difference will be that one group will use HFNO and the other group will use traditional oxygen.

Which group will use HFNO or conventional oxygen will be randomly selected from a sealed envelope. Randomised means that all participants will have the same chance of belonging to one group or another, you must choose a sealed envelope and inside it will be written to which group you will belong. You will know before of the intervention to which group you will belong.

You will have to pedal in a stationary bicycle for 30 minutes, during the other 20 minutes you will do exercises for their upper limbs using thera bands and dumbbells. Finally, you will receive 10 minutes of respiratory physiotherapy including techniques to eliminate

phlegm, breathing exercises and activities to train the respiratory muscles such as inflating balloons.

During the **Post Intervention Appointment**, you will be undergone exactly to the same tests as in the baseline appointment, except height.

Preparing for your baseline and post intervention appointment

You should continue to take all of your usual medications, unless stated otherwise in your appointment letter. You will need to wear clothes and footwear suitable for doing exercise and bring a list of your current medication with you to your appointment. On the day, you should come in well rested. It is advisable that you avoid drinks with caffeine in (such as tea, coffee, cola and energy drinks) as they may affect the results. Other fluids can be continued up to the start of the test. Do not eat a heavy meal within two to three hours of the test.

5. What are the possible risks and disadvantage of taking part?

During the bike exercises, you might experience the following: breathlessness or leg fatigue. You can stop the test at any time. Other symptoms may develop during exercise such as chest pain, drop in blood oxygen levels, drop or increase in your blood pressure however, these do not frequently happen. We will be monitoring these and we may decide to stop the test if we feel this is a risk. HFNO carries a risk of pneumothorax, nosebleeds, mucosal irritation, discomfort, etc. However, the patient can adjust the flow rate to suit them and will start off at a lower level. The study exercise tests and pulmonary rehabilitation sessions will be carried out in physiotherapy department gym located next to the respiratory ward. Therefore, equipment and appropriate staff will be readily available to assist in dealing with any emergency.

6. What are the possible benefits of taking part?

The information gained from your participation may enable us to come up with the most optimal rehabilitation programme in the future, and this may benefit patients with ILD. Your results from the assessments we perform will also be made available to you and your general practitioner with your consent. We will inform you and your GP if anything with clinical relevance is found.

7. What will happen if I do not want to carry on with the study?

You can stop at any point, but we will keep your data that has been collected up to the point of your withdrawing but no further data will be collected. This simply means that you will no longer be attending further research clinics or taking any further active part in the research. But you will still receive your usual care.

8. What will happen when the study finishes?

When the study is completed according to plan, the results may be published in scientific or medical journals or be presented at conferences and written up as part of a doctorate. Data will be stored in a long-term archive facility in the Royal Infirmary Hospital and in the Royal Victoria Infirmary during 3 years. Participants will get a copy of their results through newsletters. The tissue (blood samples) will be retained in a bio freezer in the QMRI at the University of Edinburgh for 3 years.

Figure 1: Cardiopulmonary Exercise Test (CPET)

Flowchart 1

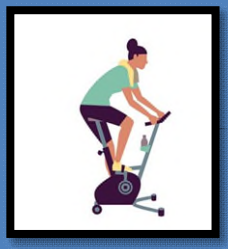
First day before the intervention (In the Clinic)	To be performed at home	First day after the intervention (In the Clinic)
•Weight •Height •Blood Test •Strength test for the thigh muscle (QMVCT) •Scale for Shortness of breath •Maximal Exercise Test on a Bicycle •Constant Exercise Test on a Bicycle •Questionnaire to measure the quality of life (SGRQ) •Questionnaire to measure anxiety and depression levels (HADS)	•Physical activity levels in daily life measured with a special belt	•Weight •Blood Test •Strength test for the thigh muscle (QMVCT) •Scale for Shortness of breath •Maximal Exercise Test on a Bicycle •Constant Exercise Test on a Bicycle •Questionnaire to measure the quality of life (SGRQ) •Questionnaire to measure anxiety and depression levels (HADS)

Intervention (In the Clinic)

Pulmonary Rehabilitation

Group 1 (Interval training + High flow nasal oxygen during 8 weeks)

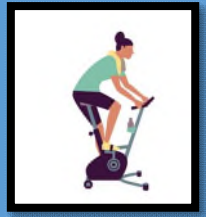
(3 times a week every other day)

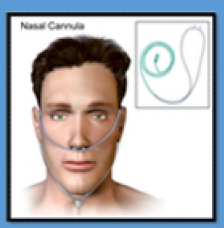


Pulmonary Rehabilitation

Group 2 (Interval training + conventional oxygen during 8 weeks)

(3 times per week every other day)





9. Expenses and payment?

You will not receive any payment for participation in this study. However, any reasonable travel and parking costs incurred by your participation during the assessment visits (baseline and post intervention appointments) can be reimbursed (up to £50). Please kindly keep any valid receipts for your claim.

10. Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws, which safeguard your privacy at every stage.

11. How will we use information about you?

We will need to use information from your medical records for this research project.

We will collect your Community Health Index (CHI) number or NHS number. Note that the CHI is a population register, used in Scotland or health care purposes. The CHI number uniquely identifies a person on the index and is personal identifiable information. Your CHI number or NHS number is being collected to allow us to check your records to make sure that the research is being done properly.

Other personal identifiable information collected will include your : initials/ name / date of birth / address / post code/ telephone number / e-mail address .People will use this information to do the research or to check your records to make sure that the research is being done properly. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no one can work out that you took part in the study.

12. What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we will not be able to let you see or change the data we hold about you.

13. Where can you find out more about how your information is used?

You can find out more about how we use your information

- At www.hra.nhs.uk/information-about-patients/
- Our leaflet available from **www.hra.nhs.uk/patientdataandresearch**
- By asking one of the research team
- By sending an email to roberto.rabinovich@nhslothian.scot.nhs.uk

- By ringing us on 0131 242 7370

Data Protection Officer contact information:

University of Edinburgh	**NHS Lothian**
Data Protection Officer	Data Protection Officer
Governance and Strategic Planning	NHS Lothian
University of Edinburgh	Waverley Gate
Old College	2-4 Waterloo Place
Edinburgh	Edinburgh
EH8 9YL	EH1 3EG
Tel: 0131 651 4114	Tel: 0131 465 5444
dpo@ed.ac.uk	Lothian.DPO@nhs.net

14. What if there is a problem?

If you have a concern about any aspect of this study please contact Dr Roberto Rabinovich (Details below) who will do his best to answer your questions.

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against NHS Lothian but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

15. Who is organising and funding the research?

This research study is sponsored by the University of Edinburgh and NHS Lothian and the funding comes from a Chilean scholarship and this research is pursuing an educational qualification.

16. Who has reviewed the study?

The study proposal has been reviewed by the research group of this study. All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from <insert REC name>. NHS Management Approval has also been given.

17. Contact for further information

In case of any questions, please feel free to contact:

Dr Roberto Rabinovich will be pleased to answer your questions.

Tel: 0131 2427370 E-mail: roberto.rabinovich@nhslothian.scot.nhs.uk

The University of Edinburgh, Queen's Medical Research Institute,

47 Little France Crescent, Edinburgh, EH16 4TJ

18. Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact:

Dr Adam Marshall. Consultant in Respiratory Medicine.

E-mail: Adam.Marshall@nhslothian.scot.nhs.uk

Tel: 01312421199

19. Complaints

If you wish to make a complaint about the study please contact:

Patient Experience Team

2 – 4 Waterloo Place, Edinburgh, EH1 3EG

feedback@nhslothian.scot.nhs.uk

0131 536 3370

This will be for NHSL participants only.

Participants from Newcastle can complain in:

Patient experience team

Email: nuth.patient.relations@nhs.net

Telephone: 0191 223 1382

You will be given a copy of the information sheet and a signed consent form to keep. Thank you for taking this time to consider participating this study.