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The Sheffield Teaching Hospitals Observational Study of Patients with Pulmonary Hypertension, Cardiovascular and other Respiratory Disease (STH-ObS): Patient Information Sheet

STH-ObS is a research study that has been established within Sheffield Teaching Hospitals (STH) since 2008. A central element of the study is a Biobank, a facility for the safe and secure long term storage of samples from patients with pulmonary hypertension, and other respiratory disease, cardiovascular disease and connective tissue disease, and a database to store information about these samples and other tests you undergo. We also collect samples from healthy volunteers for comparison. The aim of this research is to increase our understanding of the causes of these conditions, how they cause symptoms and illness, and help us to develop new ways to diagnose, treat, and prevent diseases. In some cases we may ask if you wish to participate in a study to collect activity or health and symptom related data via your mobile device (e.g. iPhone) or fill in some questionnaires. With your permission, data will be collected to help researchers understand patterns in your activity and information about your cardiovascular health. We may also notify you of other linked research projects, taking part in these are completely up to you.

Why have we asked you to take part?

You are being asked to take part because you are attending hospital with a possible or confirmed diagnosis of pulmonary hypertension (PH), or another respiratory (including COVID-19), cardiovascular or connective tissue disease which can often be misdiagnosed or associated with PH. We wish to obtain samples and data from these groups of patients for research.

What are we asking you to do?

1. We are asking you to give blood and potentially saliva, urine and nose/throat swab samples to help our research.

2. Some patients with certain illnesses may have a lung or heart/lung transplant in the future: if this happens then we would like to ask permission to obtain samples of tissue from the organ removed during the transplant.

3. We would like to ask your permission to obtain the data from tests you will have, or have had as part of your routine clinical care and from other research studies you may have been involved in. All data that we collect will be stored in a secure database for use in research.

4. We may ask if you would undertake some additional research tests (described below) but you do not have to do these test if you do not want to.

5. There are no fixed timescales for you participating in the study. We will aim to collect samples and data from you each time you return to the hospital for a clinical follow-up visit, for as long as you are willing to be involved.

6. We may contact you ask you for additional consent to participate in studies linked to this research, this is optional.

What will happen if you agree to participate?

The first thing you will be asked to do is give your written consent by signing the form attached to this information sheet. Please keep this information sheet to remind you of what you were asked to do. Once you have agreed to take part, the following will happen:

DATA COLLECTION

- We will ask your permission to obtain data that is collected during your normal clinical care and other research projects that you have been involved in (where ethical approval allows this). This will include information about your condition, other diseases, previous assessments and treatments, test results, and images (such as X-ray, CT or MRI scans). The research team will collect this data from your medical

records, and store it in a secure research database at the Royal Hallamshire Hospital. We will use this data in research.

- We would like you to give permission for regulatory authorities or officials from STH or University of Sheffield to have access to your medical notes and any data we collect for monitoring purposes.

BLOOD SAMPLES

- We will collect blood samples from you over the course of your illness. Wherever possible, we will collect blood for research every time you come to hospital for a clinical review visit. Blood will be taken at the same time as clinical blood samples. This will be like any other blood donation and should not harm you. You are free to refuse to give a repeat sample and your clinical care will not be affected.

- No more than 100ml (6 tablespoons) of blood will be taken for research at any one time and no more than 100ml (6 tablespoons) will be taken for research in any 24 hours. This will be in addition to any blood that you have to give for clinical purposes.

NOSE or THROAT SAMPLES

- We may ask you for a nose or throat swab at your visits. For example, if in future if you have another illness related to COVID-19 we will ask to take another swab to test for the virus.

SALIVA and URINE SAMPLES

- We may collect saliva and urine samples while you are in hospital and may request additional samples each time you have a clinical follow-up visit.

TISSUE SAMPLES

- If in the future you ever have a heart and/or lung transplant at a Transplant Centre (e.g. Manchester, Newcastle or Papworth Hospital), the transplant team may store tissue obtained during the procedure. If this happens, we may contact the transplant team to obtain some of that tissue to be able to analyse it alongside the other information we have collected in this study.

All blood, urine and tissue samples will be stored in the Sheffield Biorepository at the Royal Hallamshire Hospital, which is a secure storage facility licensed by the Human Tissue Authority.

OPTIONAL ADDITIONAL RESEARCH TESTS

There are several different tests we may want to perform and <u>you can give your permission to have all, some, or none of these performed.</u> Your clinical care will not be affected in any way. Details of these tests are:

Exercise Tests
You may have these as part of your normal clinical assessment. This involves performing a series of walking tasks in a measured corridor, under the guidance of a Respiratory Physiologist or Nurse. We may ask you to perform a Cardiopulmonary Exercise Test (CPET) on an exercise bike. These tests take up to 30 minutes. We will only ask if you agree to these tests and do them if we think it is safe for you to do so. We will not ask pregnant participants to undertake strenuous exercise tests.

Magnetic Resonance Imaging
MRI is one way of obtaining pictures of lungs and other areas of the body. Most patients with PH or Lung disease will have MRI scans as part of their normal clinical assessment but we may ask you to have one of these as part of our research. The scan takes approximately 60 minutes. You lie in a 'tunnel' which holds a large magnet. Short bursts of radio waves allow the images to be created. You will hear some loud 'banging' noises during the scan which are made by the magnet.

There are only minor risks associated with MRI, and no x-rays or radiation are required. Some patients may experience claustrophobia, and if the patient becomes uncomfortable the procedure can be easily stopped. During the scan we may inject a "contrast agent" into a cannula inserted into a vein in your arm, which improves the image quality, This is used commonly in the NHS when performing MRI. The needle for this will feel like a sharp scratch. Sometimes the contrast agent can cause dizziness and light-headedness, but usually people are not aware of the contrast injection. Rarely, blood pressure can fall, which can be treated immediately with a drip. Very rarely (less than one in 1000 people) an allergic reaction to the contrast is seen. This usually includes skin rash and itchy eyes for a short time. In the unlikely event of a severe reaction, medical staff are on site and will be able to deal with this quickly.

Another type of MRI scanning that we might wish to perform involves the patient breathing in gas which improves the image quality. We may ask you to hold your breath for 15 seconds. The gas, which could be helium or xenon, is inert and harmless, and has been shown to be safe and well tolerated in people with lung disease. However you may become light-headed, drowsy or feel sick for a few seconds. We will closely monitor your oxygen levels throughout the study. We will not ask pregnant participants to undertake MRI.

Breath analysis
Using new breath analysis equipment (which is similar to a "breathalyser" test), we can analyse the different compounds in your breath. The results may yield information about health and disease which is relevant in our research. If you do this test it requires you to breathe in and out of the Breath Analyser, for up to fifteen minutes.

Mobile and Home Activity Data
We are interested in determining whether everyday activity data measured by 'smart' devices and sensors are helpful in assessing disease. We are currently working with expert partners including Stanford University, Samsung and colleagues at the University of Sheffield. A member of the STH-Obs research team will inform you about this research taking place at Stanford University, USA called "My Heart Counts" which uses a mobile App. You can download the app for free onto your iPhone or other mobile device. If you agree to participate in the MyHeartCounts study you will be given a unique MyHeartCounts study identification number. The app will collect data about your levels of daily activity. The STH-Obs research team in Sheffield will then be able to use the MyHeartCounts activity data to link it to the STH-Obs study data and make direct comparisons between hospital exercise tests and your daily activity. The Stanford University researchers will not have access to any of your clinical data.

We have similar arrangements with PAI Health to obtain heart rate data, Samsung for their ACTIVAGE programme, and investigators at the University of Sheffield for their Aequora programme. Agreement to participate in either of these studies may involve the receipt of smart devices and/or home sensors which would be installed in your home (with your consent) by authorised specialist installers.

If you are interested in being contacted please provide your email address on the consent form. This will be stored securely by the STH-ObS study team. If you agree to participate in home or activity sensing tests, the study team will contact you provide you with further information about these studies and how to get involved.

No one other than the STH clinical team and the STH-Obs research team will have access to your clinical data.

Health-related questionnaires, interviews and applications
Questionnaires are standard tools used in clinical practice and research. We may ask you to complete questionnaires that are used to understand how well you are feeling, physically as well as mentally. The results will be analysed and related to the other measurements of your health and activity.

If you agree to be contacted for this purpose, we may want to contact you for a short interview to understand your experience of your health and symptoms, healthcare and research in further detail. Any interview scripts and themes will be approved by the ethics committee and taking part in this is completely optional.

We may ask you to participate in other studies which collect health related data through a smartphone application, if you choose to do this we can link this data to STH-Obs using your unique ID.

USE OF SAMPLES AND DATA IN RESEARCH

The samples and data that you donate will be stored indefinitely, for as long as we have the required ethics and research governance approval to undertake this research.

Researchers may request access to the samples and data that we have collected from you and other participants.
A Scientific Advisory Board will review applications for samples and data to ensure the research meets appropriate standards. If the request is approved, we will provide the samples and data to the researchers. We may share samples and data with clinical, academic, or commercial institutions, from inside or outside the UK.

No readily identifiable information will be given to the researchers, meaning that you nor other participants cannot be identified from the information given. When the STH-ObS provides samples to researchers they are obliged to only use the samples for the research they said they would do. Researchers will be bound by a Material Transfer Agreement reviewed by the Sponsor R&D Department.

Data Protection Information
The University of Sheffield (TUOS) is the sponsor for this study and will act as the data controller. This means that TUOS is responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at https://www.sheffield.ac.uk/govern/data-protection

Staff from the Sheffield Clinical Research Facility, as well as research team members from the University of Sheffield, may use your name and contact details to contact you about the study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from TUOS and regulatory organisations may look at your medical and research records to check the accuracy of the research. The only people in TUOS who will have access to information that identifies you will be people who need to contact you about the study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. TUOS will keep identifiable information about you for 15 years after the study has finished.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

What will happen if you say no?

You are free to decline to participate in this research. Your decision will NOT affect the care you receive from the hospital or doctor, now or in the future. If you say no, we will not take samples or data from you other than for normal clinical care. We may ask you to help us understand why you said no – but you do not have to tell us.

What happens if you agree to participate but then wish to withdraw from participation?

You can withdraw from the study at any time by contacting the research team (details given below). We will ask you to sign a "Withdrawal of Consent Form" so we can keep a record of anyone who has withdrawn. If you request that you no longer want any of the samples you have previously donated to be used in research, all samples in remaining in storage will be destroyed. If you wish to withdraw your consent, it is possible that some or all of the samples may have already been used by researchers.

What are the benefits to you?

The samples and information that you give will be treated as gifts that could help research to benefit those affected by disease in the future. It is unlikely you will benefit directly from the research as it usually takes many years for research to produce medical advances. The results of research tests involving you as an individual will NOT be put in your health records or told to you, your relatives or your doctors because the researchers cannot identify who you are. However we will publicise the research findings from the tissue bank as a whole on the websites www.lungsheffield.org, the University of Sheffield website https://medicine.dept.shef.ac.uk/news/index.php/2015/07/21/the-pulmonary-hypertension-blood-biobank/ , and the Donald Heath Research Programme website (https://donaldheath.org/home/research/). Findings will also be publicised at research conferences and via publications in academic journals.

What are the risks to you?

There are NO significant risks to donating samples for this research. There are no more risks of giving blood for research than there are for being a blood donor or giving a routine blood sample. If you are allowing us to use tissue samples, these would be collected during a transplant that would be taking place for clinical reasons.

Your clinical and research teams will take every precaution to prevent researchers from obtaining information that identifies you. The only people who will know your identity are the hospital staff and trained research staff dealing with patient records who are bound by a professional duty to protect your privacy.

Other things you should consider

The samples and information you have gifted will be made available to researchers in the UK or overseas, in universities, hospitals or private companies that do medical research. This research will always be relevant to understanding how the body works, which may eventually help understand PH and associated conditions. You will not receive any personal financial reward for making your gift.
Sometimes samples are used for genetic research about diseases that are passed on in families. However any genetic results about an individual will not be revealed to that individual. Your samples will not be used for research involving animals or reproductive cloning.

What if I have any questions or concerns?

If you have questions about this research, please ask a member of the study team by emailing sth.obs@nhs.net, research nurse, or your consultant:

Research Nurses:
Sister Amanda Creaser-Myers or Sister Sara Walker

Clinical Research Facility, O Floor, Royal Hallamshire Hospital, Sheffield, S10 2JF. Tel 0114 271 3339

Local consultant:
Prof David Kiely, Pulmonary Vascular Disease Unit, M Floor, Royal Hallamshire Hospital, Sheffield, S10 2JF
Tel 0114 271 2132

What if there is a problem or if I wish to make a complaint?
If there is a problem, please contact the study team (details above).
If wish to complain formally, you can write to:
Professor Christopher Newman, Dean of the Medical School, University of Sheffield Medical School, Beech Hill Rd, Sheffield S10 2RX.

If you are harmed during the course of the study and this is due to someone's negligence, you may have grounds for a legal action for compensation against the employing NHS Trust, but you may have to pay your legal costs. The normal NHS complaints mechanisms will still be available to you.

The Sheffield Teaching Hospitals Observational Study of Patients with Pulmonary Hypertension, Cardiovascular and other Respiratory Disease (STH-ObS): Patient Consent Form

Thank you for reading the STH-Obs Patient Information Sheet. If you would like to take part, please give your consent by putting your initials in the box labelled "Yes" after the questions below. Then sign and date the form and have this witnessed by a member of the research team.

1. I have read and understand the document "*The Sheffield Teaching Hospitals Observational Study of Patients with Pulmonary Hypertension, Cardiovascular and other Respiratory Disease (STH-ObS): Patient Information Sheet version 9.1 dated 11/12/2020*", and have had the opportunity to ask questions. These questions have been answered satisfactorily and I understand the risks and benefits of giving my samples and clinical information to STH-ObS.

   Yes ☐ **Initials** **No** ☐ **Initials**

2. I give permission to the STH-Obs study team to collect blood, saliva, nose/throat swab and urine samples from me to be used for research.

   Yes ☐ **Initials** **No** ☐ **Initials**

3. I give permission to the study team to obtain, for the purpose of research, tissue samples that have been collected from me during lung transplantation procedures, should they be required.

   Yes ☐ **Initials** **No** ☐ **Initials**

4. I understand that my blood and tissue samples may be used for DNA analysis in this research, and that only the research team will have access to personal data linked to DNA analysis.

   Yes ☐ **Initials** **No** ☐ **Initials**

5. I give permission for information about me found in my clinical, medical, other health-related records or other data from other research studies I am participating in (where the relevant approvals are in place), to be supplied to the STH-ObS study team and stored on a secure study database for research purposes. I understand this includes test results and information that has been collected previously, or will be collected in the future, as part of my normal clinical care or research.

   Yes ☐ **Initials** **No** ☐ **Initials**

6. I give permission for STH-ObS to store the samples, the clinical information collected during my normal care, and any additional information obtained during additional research tests, and distribute them to researchers whose work has ethical approval and is deemed by the STH-Obs Scientific Advisory Board to be high quality appropriate medical research.

   Yes ☐ **Initials** **No** ☐ **Initials**

7. I understand that STH-ObS will keep this information confidential at all times and that researchers will not be able to identify me from any of the samples or information that they receive.

   Yes ☐ **Initials** **No** ☐ **Initials**

8. I understand that giving samples and information for research is voluntary, and that I am free to withdraw my approval for use of the samples or information at any time without giving a reason, without my medical treatment or legal rights being affected.

   Yes ☐ **Initials** **No** ☐ **Initials**

8. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give my permission for these individuals to have access to my records.

Yes ☐ **Initials** **No** ☐ **Initials**

9. I understand that I will not personally benefit, financially or otherwise, from my gift of blood, urine, tissue, or clinical data.

Yes ☐ **Initials** **No** ☐ **Initials**

10. I agree to be approached by the study team for other research studies *(optional)*.

Yes ☐ **Initials** **No** ☐ **Initials**

OPTIONAL ADDITIONAL TESTS

11. I am interested in being contacted to find out more about additional/future mobile and health activity tracking applications.

Yes ☐ **Initials** **No** ☐ **Initials**

12. I agree to undertake additional exercise tests for the purpose of research, including walking tests or cardiopulmonary exercise tests, if it is safe for me to do so. I understand that I can choose to not undertake these tests at any time.

Yes ☐ **Initials** **No** ☐ **Initials**

13. I agree to undertake additional Magnetic Resonance Imaging scans for the purpose of research. I understand that I can choose to not undertake these tests at any time.

Yes ☐ **Initials** **No** ☐ **Initials**

14. I agree to undertake additional Breath Analysis tests for the purpose of research. I understand that I can choose to not undertake these tests at any time.

Yes ☐ **Initials** **No** ☐ **Initials**

15. I agree to undertake health-related questionnaires for the purpose of research. I understand that I can choose to not undertake these at any time.

Yes ☐ **Initials** **No** ☐ **Initials**

16. I agree that I may be contacted to have an interview to share my experience of health-care, symptoms and research. I understand that I can choose to not undertake these at any time.

Yes ☐ **Initials** **No** ☐ **Initials**

Preferred email address for contact by the study team (optional):_____

Please proceed to sign this form on the next page.

Name of Participant	**Date**	**Signature**	**Biobank ID**
Name of Person Witnessing Consent (if applicable)	**Date**	**Signature**	**Role**
Name of Study Team Member Taking Consent	**Date**	**Signature**	**Role**

Thank you for agreeing to make this gift to help research.

Create 3 copies - One for patient notes, one for participant, one for site file.