



ADULT PARTICIPANT INFORMATION SHEET

TITLE: Exhaled Breath Metabolomic Biomarkers in the Acutely Breathless Patient.
Short title: EMBER Study

Chief Investigator: Prof Salman Siddiqui

Other Investigators: Prof Chris Brightling, Prof Tim Coats, Dr Hitesh Pandya, Prof Andy Wardlaw, Prof Mick Steiner, Dr Neil Greening

Invitation

We are inviting you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it involves. One of our team will go through the information sheet with you and answer any questions you have. Please take time to read this information sheet and discuss it with others if you wish.

What is the purpose of the study?

We realise that being admitted to hospital with acute breathlessness due to heart or lung disease is an important event for both you and your disease.

We do not fully understand the causes and the factors that help the recovery of a flare up of heart or lung disease but if we can find out, it will help to design better treatments for the diseases.

We are looking for breath biomarkers of asthma, COPD, heart failure and pneumonia to identify

1. Risk of readmission and/or death
2. Response to treatment given as part of your usual care
3. Disease identification

Why have I been invited?

You have been invited to take part because you have a heart or lung condition (heart failure, asthma, COPD, pneumonia). You may also have been admitted to hospital with a “flare-up” (exacerbation) of any of these conditions.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to take part you are free to withdraw from the study at any time and without giving a reason. If you do not take part, or if you withdraw from the study, this will not affect the standard of care you receive

What will happen to me if I take part?

The study involves having some tests and collecting samples. If this is while you are unwell the tests will be done during your stay in hospital and once recovered, within 6 months. We understand that you are currently unwell in hospital and the tests have been kept short because of that. If you are well at your first visit we will see you up to a total of three times over the next 6 months. These visits can vary in time and this will be discussed with you at the time of you volunteering as they will be guided both on your flexibility, how you are feeling and our study requirements.

We would like to collect and analyse samples of breath, blood, sputum, urine and take measurement evaluating your health using questionnaires of lung function with breathing tests, leg muscle and walking function during your hospital stay and once recovered.

The study involves having some tests early in your hospital stay and possibly some different tests before you go home once you are feeling a little better. You will then have some more tests when we see you in clinic, once you have recovered from your current illness.

Before taking part in the study, you will be asked to sign a form saying that you agree to take part.

If you agree to take part, you will be asked to sign the consent form.

The tests you may be asked to perform are outlined below:

Medical history, physical examination and questionnaires: We will ask you about your previous medical history and any current medical problems that you may have. We will ask you about medications that you are taking and a record of your smoking history. We will get some of this information from your medical notes. You will be asked to fill in questionnaires regarding your respiratory symptoms, feedback on some of the tests performed and your quality of life. The number of questionnaires you complete will be determined by your disease and can range from one to five. This will be completed at every visit.

Blood Collection: Along with the blood samples taken routinely you will be asked to provide an additional blood sample during your hospital admission and once you have recovered (which can take up to 6 months). These samples will measure your general health, biomarkers and the genetics of your condition. We will not take any more than 85mls of blood per visit (this is equivalent to about 5 tablespoons). This may cause some mild discomfort and occasionally some bruising.

Sputum Collection: Sputum is the substance that is brought up from the lungs when a person coughs or spits. We can study sputum in the laboratory to measure the types of cells, inflammatory chemicals and organisms in it. If you cannot bring up any sputum you may need to inhale a salty solution. This test is called induced sputum or sputum induction. For this test we will perform spirometry. Spirometry is a type of lung function test which involves breathing out as hard as you can several times, repeated once more after inhaling Ventolin. Once we have your spirometry measurements you will then inhale the salty solution for three 5-minute periods. In between these 5 minute periods you will be asked to perform a spirometry measurement to check your symptoms. This test can cause some chest tightness, wheezing and/or cough. These can all readily be reversed by inhaling a bronchodilator (salbutamol via a nebuliser or inhaler and spacer). In order to monitor this, Spirometry will be performed before and during this test. Sputum will be collected at each visit.

Urine sample: A sample of urine will be collected at each visit.

Breathing Tests: You may be asked to do 3 different types of breathing tests if you are well enough.

- **BREATHING TEST 1 (Spirometry):** If able to do so, we will ask you to you empty your lungs as hard and fast as you can through a tube several times. You may have this repeated once more after inhaling Ventolin. This device will take two measurements; the amount of air you can breathe out in one second (forced expiratory volume in 1 second, FEV₁) and the total amount of air you can breathe out (FVC). This takes approximately 15-30 minutes.
- **BREATHING TEST 2 (Exhaled Nitric Oxide Test):** This is a simple breathing test that involves breathing slowly into a machine to look for airway inflammation. This takes no longer than 5 minutes. This is a breath test which measures the amount of nitric oxide that is exhaled from your lungs. The amount of nitric oxide exhaled can provide an indication of the degree of inflammation present in your lungs. You will be seated and will be asked to fully inhale, and then exhale slowly for at least 10 seconds through a mouthpiece.
- **BREATHING TEST 3 (Breath Collection):** We will ask you to breathe with a mouth piece or mask over your nose and mouth directly into breath sampling devices. This testing may take up to 30 minutes in total and breath samples will be collected while you breathe. If you require oxygen to support your breathing as a result of your flare up, this will be supplied. During the test, you won't be able to talk but you can write messages. There will always be someone with you who can stop the test at any time if it's uncomfortable. These tests are designed to look at the chemicals in your breath and to see whether breathprints derived from breath samples can identify the nature of the flare up that you have had.

In addition we will perform other breathing tests such as:

- Oscillometry is a simple breathing test where you breathe normally into a device that measures the effect of sound impulses on your lungs.
- Peak flow measurements

Some of the breathing test (spirometry and peak flow) may cause some temporary light headedness, and coughing.

Walking tests:

We will ask you to walk 4 metres at your own pace twice. It takes approximately 3 minutes to complete.

Quadriceps Ultrasound:

We will measure the size of your quadriceps muscle using ultrasound. This is a non-invasive scan where we apply a gel and gently place a probe over your leg to get a picture. This will be done whilst you lie in your bed and takes about 5 minutes.

Health Care Use

We will use hospital and GP records to monitor any further admissions to hospital or further treatment for exacerbations prescribed by your GP for 2 years after your admission to hospital.

Other tests such as ECG, Chest x-ray, Echocardiogram may be performed as part of your routine clinical care and the results of these tests will be accessed and used in this study. For patients where there is no clinical indication for an [Echocardiogram](#) a research [Echocardiogram](#) may be performed.

What do I have to do?

As this is an observational study and there is no difference from your normal treatment then you do not need to do anything different from normal, other than agreeing to perform the tests described above.

What are the possible disadvantages and risks of taking part?

There are minimal identified risks to taking part in this research. All participants will have blood samples. There may be minor discomfort and bruising at the site where the needle is inserted. All blood samples will be taken by a doctor or fully trained health professional. Some of the breathing test (spirometry, peak flow & induced sputum) may cause some shortness of breath, temporary light headedness, and coughing, however these are short lasting effects and should resolve.

What are the possible benefits of taking part?

It is unlikely that this study will directly help you but the information we get from this study will help improve the treatment of people with heart and lung diseases.

What will happen if I don't want to carry on with the study?

You are free to withdraw your consent to participate in the study at any point, if you wish. This can be done by contacting a member of the research team (either in person, or using the telephone number at the end of this information sheet). You do not have to give a reason if you wish to withdraw and it will have no effect on your future treatment. If you are unable to provide consent at any time during the study (lose capacity), you will be withdrawn. In both cases any information or samples collected up until that point may still be used in the study. These samples will not have any personal information that can identify you.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions (0116 258 3370). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Please contact the Patient Information and Liaison Service (PILS), Tel: 08081788337.

In the event that something does go 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 but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it. With your consent your GP will be notified of your taking part in this research.

During the study, your samples and any data collected about yourself will be labelled with a participant number, not your name. This number will be in place of any identifiable information. Only your study doctor and some members of the clinical study team directly involved in the study will be able to link your subject number to your name. Your study data will be stored on paper and on a computer database. These records will be kept separate from your medical records. Your consent to the use of Study Data does not have a specific expiration date. Your medical records and previous tests performed to assess your respiratory condition (eg. breathing tests) may be reviewed by research staff working on the study for the purposes of research. This previously collected and prospectively collected clinical information may be utilised in an anonymised fashion for the purposes of research into lung and heart diseases. Your medical records and study data may also be looked at by representatives of the NHS and the sponsor for monitoring and auditing purposes to check that the study is being carried out correctly.

Your study data and samples may also be shared with our research collaborators in other academic institutions, industry partners and pharmaceutical companies. Any of your data or samples that are shared with such persons will be anonymised. The Study Doctor's institution and our research collaborators in other academic institutions and pharmaceutical

research companies are each responsible for their handling of Study Data in accordance with applicable Data Protection law(s). The Hospital and our research collaborators in other academic institutions and pharmaceutical research companies may transfer Study Data to countries outside of the UK and the European Economic Area (EEA) for the purposes described in this document. Please be aware that the laws in such countries may not provide the same level of data protection as in the UK and may not stop Study Data from being shared with others. However, rest assured that all Study Data that is transferred would be coded, so your identity is masked.

Involvement of the General Practitioner (GP)

We would like to notify your GP that you have agreed to take part in this study and will ask your permission to do this. They will not receive individual results of the research specific tests completed unless they have an impact on your care.

How will my samples be used?

All the samples you have donated will be used in research by the Hospital and our research collaborators in other academic institutions and pharmaceutical research companies. Samples may be stored and used for future research, which may be shared with collaborators in the UK, EU and outside of the EU. All data and samples will be anonymised i.e you will not be personally identified by this information.

All the testing of your samples, now and in the future, will be performed for research and development purposes only. Any information derived directly or indirectly from this research or any optional future research, as well as any patents, diagnostic tests, drugs, or biological products developed, will belong to the researchers. The results from this research and any future research may be used for commercial purposes. You will have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this or any future research. However, in signing this form and donating sample(s) for this and any future research, you do not give up any rights that you would otherwise have as a participant in such research.

You may withdraw your consent to participate in the study at any point; however, if you withdraw your consent then the information collected up until that point may still be used in the research and may still be shared with our research collaborators in other academic and industry partners. If any analysis has already been performed then neither we nor our research collaborators in other academic institutions and pharmaceutical research companies are obliged to destroy the results of this research.

Will any genetic tests be done?

We would like to analyse the genetic patterns in the inherited material that may be linked to an increased risk of developing airway and heart disease. This is preliminary work which would not affect insurance status or be used to give information for other family members and therefore the results will not be made available to you. There is a separate section to sign on the consent form if you will allow us to analyse your blood for genetic patterns. Any incidental findings from this test will not be disclosed to participants.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favorable opinion by the Leicester Research Ethics Committee. The study has also been reviewed by the University of Leicester as the study sponsor.

Who is organising and funding the study?

This study has been funded by the Medical Research Council (MRC) & Engineering and Physical Sciences Research Council (EPSRC) and is sponsored by the University of Leicester. The children's component of this study is also being supported by The Midlands Asthma and Allergy Research Association (MAARA).

Expenses and payments

Travel and car park charges will be reimbursed for all healthy volunteers and for patients who are invited back for any research specific visits. Mileage will be paid at 40p/mile. Please retain receipts for car parking charges. Reimbursements cannot be made for routine clinical care i.e. out-patient clinic appointments or readmissions.

What will happen to the results of the research study?

The results of this study may be communicated in talks and via articles in journals. We do not intend to provide direct feedback about the study to participants. However, if you wish to know the information relating to results of the study, you can do so by contacting the chief investigator, Prof Salman Siddiqui or the research team.

Further information?

You may contact **The Ember Research team** on 0116 258 3370.

Thank you for reading this

Please keep a copy of this information sheet and the enclosed consent form

ADULT PARTICIPANT CONSENT FORM

Participant ID:

IRAS Number: 198921

Sponsor Ref: UNOLE 0569

TITLE: Exhaled Breath Metabolomic Biomarkers in the Acutely Breathless Patient.

Short title: EMBER Study

Name of Investigator: Prof Salman Siddiqui

Please initial box

1. I confirm that I have read and understand the adult participant information sheet dated 01-Apr-18, Final version 4 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. I may be withdrawn from the study if I am unable to give consent for any reason (lose capacity). I understand that should I withdraw or be withdrawn, then the information collected so far may still be used in the project analysis.
3. I understand that relevant sections of my medical notes and/or study data may be looked at by responsible individuals from the study team, the sponsor or the NHS Trust where it is relevant to my taking part in the research.
4. I understand that I am consenting for my anonymous samples and data, including previous clinical data, to be used in research along with anonymised data by Leicester Glenfield Hospital, academic & industry partners. These may involve samples being sent to other centres, both in and outside the EU.
5. I agree to donate as a gift the samples of tissue (blood, sputum, saliva, breath, urine) for research in the above project and any other ethically approved future research.
6. I give permission for my samples to be used for genetic tests. I understand it will be used to look at the patterns that may be linked to an increased risk of developing airway disease. I understand that this is preliminary work and would not affect insurance status or be used to give information for family members.

<input type="checkbox"/>	<input type="checkbox"/>
Yes	No
7. I agree to my GP being informed that I am taking part in this study.
8. I agree to take part in the above study.

Name of Participant
(BLOCK CAPITALS)

Date

Signature

Name of Person taking consent
(BLOCK CAPITALS)

Date

Signature

1 for patient; 1 for researcher; 1 to be kept with hospital notes