Study Title: 'Delivering personalised care in the management of exacerbations of chronic obstructive pulmonary disease: A multi-centre randomised clinical trial'

COPD: STudying Acute exaceRbations and Responses: a randomised clinical trial. The COPD STARR 2 Study

Chief Investigator	**Professor Mona Bafadhel**
Sponsor	**University of Oxford**
Funder	**National Institute for Health Research** **PDF-2013-06-052**

Study Invitation:

We would like to invite you to take part in a research study

Before you decide to take part, we would like to inform you as to why the research is being done and how it would involve you

Please take time to read the following information leaflet and ask any questions if you have any

Please get in touch if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part

Why are we doing the study?

We would like to treat patients with a COPD exacerbation in a personalised way. To do this we think we can use a pin prick blood test and tailor the treatment prescribed. We believe we can predict if you will respond to steroids or antibiotics by testing your blood when you are having an exacerbation. We have previously studied and shown that we can identify different sub-groups of patients with different responses to steroids and antibiotics using a simple blood test.

Why have you been invited?

You have been invited to take part in the study because you have COPD (chronic obstructive pulmonary disease). Having COPD means there is permanent damage to the lungs which stops them from working properly. Some people with COPD have times when they get worse and need to see their doctor or specialist nurse. These episodes are known as lung attacks or exacerbations. The main treatment for these lung attacks is a short course of steroids and antibiotics. Sometimes these treatments are helpful, but sometimes they do not work well. Importantly, the use of steroids can complicate heart disease, osteoporosis and diabetes. Our current inability to know exactly which treatment should be given to which patient means that not all patients are being given the most effective treatment. We are inviting you to take part in the research study to help us to answer these questions.

Do you have to take part?

No, it is entirely voluntary. Please call the study nurses and ask any questions that you may have to help you decide. If you return the reply slip and we will contact you by telephone or email. You will have the opportunity to discuss the study and ask questions before arranging an appointment. If you decline or withdraw, this will not affect your care now or in the future.

What will happen if you take part?

We will perform questionnaires, breathing tests, urine test, blood tests and a pin-prick blood test at the GP surgery when you are well and will ask you to contact the COPD STARR Nurses to see you again at the GP surgery when you are having a lung attack. At the time of a lung attack, you will be entered to one of 2 groups; one group will

receive treatment in the usual way (steroids and the antibiotic doxycycline) and the other group will have treatment of steroids guided by the blood test (steroids or placebo and doxycycline). The group you will be in will be chosen by chance and you and the site team will not know what group you have been allocated to. We would then like to follow you up at the GP surgery to see how you are progressing. This information will help us to improve the way we treat patients with COPD in the future. At the end of the study we would like to keep you informed of the results of the study and will send you a newsletter with this information and further updates. All the appointments will be undertaken at the GP surgery. Any information collected about you will be anonymous.

Female participants of child-bearing potential will be asked to use contraception and to inform the study team if they become pregnant as doxycycline is not recommended in the second and third trimester of pregnancy.

Study details

The registration visit can be performed before or after your exacerbation visit. The follow-up visits will be at 2, 4 and 12 weeks after your exacerbation visit. A telephone follow up will only take place if you are not able to attend the surgery within the follow up visit window. At 12 months, there will be a review of your medical notes.

Registration visit

The stable visit will be performed at the surgery and is anticipated to last no longer than 1 hour. The study team will:

1. Ask you some questions about your general health and about your COPD.
2. Ask you to fill out some questionnaires about your health.
3. Ask you to perform breathing tests.
4. Ask to collect no more than 10 drops of blood from a pin-prick sample.
5. Ask to collect no more than 20mLs (2 tablespoons equivalent) of blood.
6. Record your oxygen levels using a finger probe.
7. Test your urine for levels of protein, infection and sugar
8. Ask you to complete a diary card of your symptoms.

Exacerbation Visit

We would like to see you at the onset of an exacerbation or when your symptoms are getting worse and would ask you to contact us directly prior to starting any medicine. You will be seen at the GP surgery by the study team and/or your doctor/practice nurse to confirm that you are having an exacerbation. You will have assessments and the pin-prick blood test which will guide to which study arm you will be assigned. The exacerbation visit will be performed at the surgery and will take approximately 60 minutes. At the exacerbation visit, the study team will:

1. Review your medical notes about your symptoms, medication and consultation with the doctor, nurse or other members of the healthcare team.
2. Ask you some questions about your symptoms following your COPD lung attack.
3. Ask you to fill out some questionnaires about your health.
4. Ask you to perform two breathing tests.
5. Record your oxygen levels using a finger probe.
6. Ask to collect no more than 10 drops of blood from a pin-prick sample.
7. Ask to collect no more than 20mLs (2 tablespoons equivalent) of blood.
8. Test your urine for levels of protein, infection and sugar
9. Ask you to complete a diary card of your symptoms relating to breathlessness, cough, sputum colour and volume for the next 30 days.
10. Make an appointment to see you in 2 weeks

You will then be anonymously allocated to the 'Usual Treatment Group' or the 'Blood Test Treatment Group' and will receive steroids and/or antibiotics. Neither you nor the nurse will know which treatment you will be having.

- In the 'Usual Treatment Group' you will receive the equivalent of Prednisolone (30mg) once per day for 14 days and Doxycycline (200mg) once per day for 7 days.
- In the 'Blood Test Treatment Group' you will receive Prednisolone (30mg) or Placebo once per day for 14 days and Doxycycline (200mg) once per day for 7 days.

Common side effects of prednisolone (occurring in greater than or equal to 1%) include irritability, depressed mood, euphoria, anxiety, sleep disturbance, confusion, suicidal thoughts, hallucinations and aggression. Common side effects of doxycycline include

allergic reactions, nausea, vomiting, headache and photosensitivity. If you have a known allergy to prednisolone or doxycycline, you will not be eligible to enter the study.

In these groups, you will receive your treatment directly from the research nurse team. You will be monitored and additional treatment will be given if you need it by your GP or practice nurse. We will talk you through how to take the medications and what common side effects to expect (in addition to providing detailed instructions with all medication dispensed). You will also be given a study card with our contact details, should you have any questions. All your usual medication will be continued.

Follow Up Visits

These follow-ups will be to determine how your symptoms have been following your lung attack. These visits will take no more than 30 minutes. The study team will:

1. Ask you some questions about how your symptoms have been since your lung attack
2. Review your diary card
3. Ask you to perform a breathing test
4. Record your oxygen levels using a finger probe
5. Ask to collect no more than 10 drops of blood from a pin-prick sample
6. Ask to collect no more than 20mLs (2 tablespoons equivalent) of blood.
7. Test your urine for levels of protein, infection and sugar
8. Review your medical notes about your symptoms, medication and any consultations which you may have had with the doctor, nurse or any other members of the healthcare team you may have contacted.

Study assessment information

Measuring oxygen levels

A probe will be placed on your finger for 10 seconds to record your oxygen levels.

Breathing tests

First you will be asked to take a deep breath and then blow hard into a machine for 10 seconds. You will then be asked to blow into a machine several times to measure the capacity of your lungs. This is called spirometry and is the test you will have previously

performed to confirm you have COPD. Secondly you will be asked to blow in a more controlled manner into a FeNo machine which measures inflammation in your lungs by analysing your breath.

Questionnaires

The questionnaires are designed to measure your overall health, symptoms and quality of life. Each questionnaire will take a maximum of 5 minutes to complete. There will be up to 5 questionnaires to complete. The study team will go through each questionnaire and answer any questions you may have. The same questionnaires will be used for the telephone visit. You will also be asked to complete a daily symptom diary for the study team for 30 days after your exacerbation visit.

Pin-prick blood test

A very small volume of blood (up to 10 drops) will be taken from your finger, also called a pin-prick test, to measure cells in the blood to inform the study doctors about your COPD and the lung attack.

Urine test

A sample of urine will be tested for levels of protein, sugar and any signs of infection. This will then be discarded.

Venous Blood test

A maximum of 20mLs (2 tablespoon equivalent) will be taken at each visit. This blood collected into anonymised tubes and transported to the John Radcliffe Hospital.

What are the possible risks and disadvantages of taking part?

The breathing test may cause cough, chest tightness and occasional wheezing. Salbutamol (Ventolin, a reliever inhaler) can be provided to rapidly treat these symptoms. The blood samples may cause some mild discomfort but this is expected to cease very quickly. Doxycycline can cause side effects such as a stomach upset or rash. Please inform the study team if this happens. On very rare occasions, you may be allergic to prednisolone or doxycycline or the placebo. If you have an allergic reaction,

we ask that you seek medical attention straight away and let the study team know if this happens

What are the possible benefits of taking part?

You will receive no direct benefit from being involved in this study. However, the information we get from this study may be used to improve the treatment of people with COPD in the future.

Will I receive any payment to take part?

Reasonable travel expenses for any visits additional to normal care will be reimbursed on production of receipts, or a mileage allowance provided as appropriate.

Will my information be kept confidential?

All the information you provide (study data) will be kept confidential and secured abiding by the Data Protection Act 1998. If you decide to take part, you will be allocated a unique study number and only specified research personnel will have access to the code to identify your details. Responsible people from the University of Oxford, or the NHS may be given access to the study data to ensure we are complying with research regulations. The results of the study may be published in the medical literature but you will not be identified. If there is new information about the study, we will keep you informed throughout and you will always have an opportunity to ask questions throughout the research study.

What happens to any samples I provide?

With your permission, blood samples that you provide for the STARR 2 study will be used for analysis to measure inflammation and also stored to be used in future research studies. Blood samples taken at each visit will be processed at the surgery and collected into fully anonymised prepared barcoded blood tubes. These tubes will be transported to the John Radcliffe Hospital, without your personal details, and analysed and frozen for future research in the Respiratory Medicine Laboratory at the John Radcliffe Hospital. The samples may be used by commercial companies or sent abroad and will remain anonymous, without any personal identifiable details now or in the future.

What happens if you want to stop taking part in the study?

You are free to stop taking part in the study at any time without giving a reason. This will not affect the medical care you receive now or in the future. If you would like to withdraw from the study, we will use the data collected up to your withdrawal. Please contact the research team to inform us of your choice.

What happens if there is a problem or if something goes wrong?

If we find anything unexpected, we will let you and your GP know to clinically verify and manage if required. If you have a concern about any aspect of this study, you should ask to speak with the research team who will do their best to answer your questions. Their contact details are given at the end of the document. If you remain unhappy and wish to complain formally, you can do this by contacting the research team or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224 or the head of CTRG on email at ctrg@admin.ox.ac.uk. The University of Oxford has arrangements in place in the unlikely event that harm arises to you from taking part in this research study. The normal National Health Service complaints mechanisms are available to you. National Health Service indemnity is available in respect of clinical treatments that are provided during your participation in this study.

How have patients and the public been involved in this study?

In designing this study, we have taken into account patient opinions on the study, study design and the tests we will carry out.

Who is organising and funding the research study?

The study is being organised by Professor Mona Bafadhel, funded by the National Institute for Health Research (NIHR) and sponsored by the University of Oxford.

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 favourable opinion by the London Fulham Research Ethics Committee.

Participation in future research

We would like the opportunity to contact you for participation in future studies that may be of interest to you. Agreeing to this, does not mean you have to take part. If your do agree to be contacted in the future, your personal details will be stored in a secure, password protected database at the University of Oxford and only accessed by delegated members of the research team.

Thank you for taking the time to read this information

Please ask if you have any further questions

Contact details:

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