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The use of a personalised early warning decision support system with novel saliva bio-profiling to predict and prevent acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD) - 'Predict & Prevent AECOPD'

Patient Information Sheet

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Summary of Predict&Prevent AECOPD Study

We would like to invite you to take part in the **Predict&Prevent AECOPD Study**. The study asks if an App called 'COPDPredict™ BASIC', can be used by patients with COPD, at home, to;

- improve self-management
- help them predict "flare ups" early
- take early action to avoid hospitalisation.

- Joining the study is voluntary and your participation should be freely given but before you decide, we would like to provide you with information about why the research is being done and what it will involve. If you decide to take part you are still free to withdraw at any time, without giving a reason. Any decision you make will not alter your normal treatment plan or after-care. Please take time to read this information sheet fully. It will provide you with information about the study and what will happen to you if you wish to take part.
- You will have the opportunity to discuss the study with a member of the research team and there will be time to ask any questions you may have.
- Please feel free to talk to others about the study if you wish.

What is the purpose of the study?

Patients with COPD have daily symptoms of breathlessness, cough and/or sputum production. These symptoms can progress and be made worse by flare-ups (called exacerbations), during which breathlessness increases and daily activities become more difficult to perform. If not suitably treated, these flare-ups can progress further so that a stay in hospital may be necessary.

There is no reliable solution at the moment that can help to monitor patients with COPD and predict when these flare-ups are going to occur.

The aim of our study is to try a monitoring solution which consists of a patient App (COPDPredict^{TM} BASIC) which combines information from symptoms, breathing tests (spirometry) and blood/saliva measurements that patients with COPD can perform at home, in conjunction with a web based dashboard for a nurse/doctor (research team) to monitor patients. This App will allow a patient to view their progress, receive information of a change in their health such as possible flare-ups and respond to self-management and treatment plans.

The dashboard will allow the research team to have access to patient information, monitor a patients' health and also provide treatment recommendations via messaging, telephone or if necessary, to organise a nurse-led home visit. Hopefully this will prevent serious problems from developing and admission into hospital.

Why have I been invited?

You are invited to participate in this study as you have a condition called COPD and have either already had to stay in hospital due to a flare-up in the last year, or have more than two less serious COPD flare-ups in the last year. The study will require 384 patients, who have frequent flare-ups, to be identified from a number of hospitals.

What will happen to me if I choose not to take part?

Whether you choose to enter the study or not you will be provided with standard advice by a nurse about how to know when you are having a flare-up and what to do when you have one. You will be also be provided

with a prescription for some medication (antibiotics and steroids) to be used according to the standard advice given by the nurse.

Depending on the symptoms you are experiencing at the time, the advice will be;

- Just monitor your symptoms to see if they are getting worse
- Start taking only the antibiotics
- Start taking only the steroids
- Start taking both the antibiotics and steroids

Whether you choose to enter the study or not, how you manage your symptoms will always be one of these four options above but what you will be asked to do next depends on if you choose to enter the study.

What will happen to me if I take part?

If you agree to take part in the study, we will ask you for your written consent at the first visit. This first visit may be;

- **At the end of a stay you've had in hospital or had a flare up in the last 6 weeks**. If you enter the study in this way, you will need to fully recover before we ask you about the level of symptoms you're having
- **During a standard visit to outpatients to check your COPD and have not had a flare up in the last 6 weeks**. If you enter the study in this way your care team may start the tests below during this outpatient visit
- **Following a letter inviting you to attend a clinic meeting**. If you've been invited to enter the study in this way you will have to visit your care team to do the procedures mentioned below.

If you choose to enter the study we will ask about your general health, perform a simple breathing test to determine your lung volumes and obtain a small sample of blood to test for C-Reactive Protein (CRP) a marker of infection. The breathing test will be performed using a standard portable machine called a spirometer; the blood test will be performed using a portable blood analyser. As these are common tests you may already have had similar tests in the past at your GP surgery or

as a healthcare check. The tests each take less than five minutes to perform.

We will also inspect the inside of your mouth and gums to make note of any infection.

If you do choose to enter the study you will then be “randomised” to either the current standard self-management of your COPD symptoms (the Control Group) or to use the App to help with doing this (the Intervention Group). Randomisation is a method based on chance by which study participants are assigned to an intervention group and is a more reliable way of being sure that the results of the study will apply to other people with COPD. By entering the study you are agreeing to be randomised to one of the following:

- **Control group** – you would continue with your standard self-management plan and attend your routine appointments. You will be asked to answer some questions by a Research Nurse over the phone, or at the same time as your regular appointments, every three months for a year (five times at the most).
- **Intervention group** – instead of your standard self-management plan, we will ask you to provide regular information about your health using the App on a tablet computer. The information will only be available to view by you, and the research team. As in the control group, you will be asked to answer some questions by a Research Nurse over the phone or at the same time as your regular appointments every three months for a year (five times at the most).

For the Control Group – standard self-management

Whichever way you enter the study, as an in-patient, out-patient or via a letter invitation, you will then start the self-management plan and will be monitored via a phone call by the Research Nurse at three and nine months. The telephone interview should take no more than ten minutes to complete and the questions you are asked will be the same for all study patients. The questionnaires have been carefully designed with the help of patient and public involvement to cause as little burden as possible, but they are in addition to your usual care. As a thank you for

completing the questionnaires we will offer you a £10 voucher, for use in selected high street stores.

Standard care for all patients with your diagnosis to attend a 12 month review in a hospital, but we are asking all patients to attend a six month review at the hospital in addition to this and you can claim your travel expenses for this additional visit, should you wish. At both of these hospital appointments the care team will ask you some questions about your health generally and your COPD symptoms.

We will also ask all patients who enter the study if they are willing to be contacted again, so that we can have an in depth discussion with them ("research interview") about their experience of coping with their COPD and participating in this study. Only around 30 patients who agree to be interviewed in this way, will actually need to be contacted. If you agree, and we do contact you, you will have a further chance to ask questions about what is involved before you decide to participate.

With any aspect of the study you can always change your mind and it will not affect any other aspect of your care.

For the Intervention Group – App and Dashboard

You will be given an information leaflet on the App, a tablet computer pre-installed with the App, a portable hand-held spirometer and some saliva collection tubes (shown below) to take away with you.

Spirometry – Vitalograph Lung Monitor

Saliva Collection Sal'Clenz/ 15ml Centrifuge Tube

You will be provided with a tour of the App and shown how to record your symptoms though a simple wellbeing diary, perform spirometry, access a self-management plan, send messages, read alerts on your health and educational information on the App.

The App also contains comprehensive instructions which you will be shown how to read on the tablet computer. You will receive reminders to use the App and make regular collections of your saliva. The reminders will be in the form of a message notification which will “pop-up” on the screen of the tablet computer.

When you submit your data on the App, based on your answers the system may provide advice via a “pop-up” messages on how to manage your condition. This may involve further spirometry, a blood/saliva test and/or a change in your health and you may be sign-posted to a section of the App on how to manage your condition. The reports would only be available to view by you in the App and the research team through the dashboard.

The information you have entered on the App monitored by the research team if it shows/the team decides that you need to be seen urgently, during office hours <insert office hours definition> a research nurse may contact you using your preferred method (e.g. landline, mobile) to discuss your App report.

When you start the study in the intervention group
Following randomisation, you will be asked to use the App for 2 weeks to enter your wellbeing daily, perform spirometry as shown at your first visit, to record your breath and any symptoms. During this 2 weeks you will also be asked to provide saliva samples on specific days and allow 2 blood samples to be taken in clinic. This 2 week period sets your stable baseline. At the end of the 2 weeks you should return to the clinic for a further blood sample to be taken. Staff will ask you if you have had a flare up during these 2 weeks.

Wellbeing Diary
You will be shown how to access a simple wellbeing diary on the provided tablet computer. We will demonstrate how to complete and submit it daily. Instructions are provided in the App and you will be shown how to access these. The electronic wellbeing diary involves scoring from 1 to 5 how you are feeling, how bad your cough and sputum production is and the colour of your sputum. The App automatically sends an alert if you haven’t completed it for the day. The wellbeing diary will always need to be entered daily.

Spirometry
The App has been built to receive information from a handheld spirometer (which you will have been provided with at your first visit) and

after the 2 week baseline you will be asked to use this spirometer weekly or when instructed by the App so that your breath can be measured.

Saliva

We will ask all patients in the intervention group after the 2 week baseline to provide a saliva sample weekly until, or unless, instructed by the App or when you start treatment for a flare up. This will involve rinsing your mouth out with water, and then drooling saliva into one of the special containers provided at your first visit. The containers will be marked with a measure level to indicate when you have provided the required amount of 1 ml (much less than half a teaspoon). This normally takes about two minutes to perform. Once the samples are done you will need to place the containers in the provided bag and store in your refrigerator for collection by a courier. You will need to contact the courier to arrange a convenient time for collection. Full details will be provided when you have been randomised. The courier will collect samples on Monday, Wednesday and Thursday. We ask that you contact the courier for collection of saliva within 24 hours unless it's the weekend in which case collection can occur on Monday. Samples will be transported to the University Hospital of North Midlands (UHNM) Pathology lab for processing. Samples will be stored for a minimum of 10 years at either (UHNM) or an appropriate facility within the United Kingdom. We are asking you to do this so we can measure the levels of CRP in your saliva which may change at the very start of a flare up.

Blood Tests

The App will send a message when a blood test for C-reactive protein is required. A member of the research team will contact you to arrange for a test within 16 hours. If absolutely necessary (e.g. due to lack of 7 day working) a further 24 hours window will be allowed so the test can be completed in 40hours. The test will take place in your home and you will not need to attend the hospital. The blood test is a finger-prick involving several droplets of blood which will be analysed by a portable machine brought to your home. The result is available within 5 minutes and will be entered into the App by the nurse. The purpose of the blood test will be to help us to know if the changes in your saliva are the same as those in your blood because we would like, in the future, to not need to take blood samples.

If you have a flare up and you have been recording the readings on the electronic device, as above, it should cause an alert to be sent to the care team. The care team will then arrange some home visits during this

flare up. The device will also sign post you to a set of recommendations and you can decide whether you should start taking any of the study medication you've been prescribed at your first visit. The research team may also recommend that you start treatment for the flare up.

During treatment for the flare up you will continue to complete the wellbeing diary, spirometry and saliva samples as instructed by the App.

What are the possible benefits of taking part?

This study will help us to find out which level of support is better at helping patients manage their symptoms. We do not know whether using this App will help with this and there may be no immediate benefits to you; the aim is to improve the care for patients with your condition in the future.

What are the possible disadvantages and risks of taking part?

We do not know if having extra information will help you manage your illness or not – that is why we are doing the study – and we could find that having more information makes patients less sure about how to manage their illness. You will be monitored by the research team whichever group you are randomised to.

For participants in both groups, the extra information we collect for the study will take some of your time.

If you are assigned to the App group, it will take time to complete each report – about 5 minutes. The App will ask you about your quality of life and symptoms. Sometimes patients can become upset when answering these types of questions. Outside of office hours we would ask you to contact your GP if you have any concerns about your health or care after completing the App questions.

During the baseline two weeks, you will be asked to provide a pin-prick of blood on four occasions. You will similarly be asked to provide a pin-prick of blood during the study at any flare-ups you have; or when messaged by the App. These tests do prick the skin and will cause mild discomfort, very briefly, as would an ordinary pin-prick.

What happens when the research study stops?

The follow up period is 12 months in this study and this will be alongside, or in addition, to the normal follow-up you would receive from your GP. After the study visits finish, you will be followed up as normal by your named GP at your regular practice.

Who is organising and funding the research?

The study is sponsored by the University of Birmingham (meaning The University of Birmingham has accepted certain legal and ethical responsibilities for the study), is being coordinated by the Birmingham Clinical Trial Unit (BCTU) and is funded by the government through the NIHR Invention for Innovation (i-4-i) programme.

The COPDPredict™ BASIC App has been developed by a commercial company, NEPESMO.

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

Members of the Clinical Research Ambassador Group (CRAG), and other independent patient and public representatives helped to develop this research topic and the research questions that should be asked. The members of this group are lay people; however some are also co-applicants and will continue to be involved closely with the progress of the study.

In designing this study we have taken into account patient opinions on the frequency of participant visits and the tests that we will carry out.

However the conduct of the study is entirely in the hands of very experienced clinical staff and no lay person has any access to your personal health or care records or is able to influence your treatment.

Who has reviewed the study?

All research which takes part in the NHS is looked at by an independent group of people which protect the patient interests. This group is called a Research Ethics Committee (REC) and **Predict&Prevent AECOPD** has been reviewed and given a favourable opinion by London-Stanmore Research Ethics Committee.

Will my taking part in this study be kept confidential?

All information collected about you for this study will be subject to the General Data Protection Regulation and Data Protection Act 2018 for health and care research and will be kept strictly confidential.

University of Birmingham is the Sponsor for this study. The University of Birmingham will be using information from your medical records in order to undertake this study and will act as the data controller for this study. This means that the University of Birmingham are responsible for looking after your information and using it properly. University of Birmingham and the NHS will keep identifiable information about you for at least 25 years after the study has finished, to allow the results of the study to be verified if needed.

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.

The NHS and the University of Birmingham will use your name and contact details to contact you about the research 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 the University of Birmingham and regulatory organisations may look at your medical and research records to check the accuracy of the research study. <NHS Trust> will pass these details to University of Birmingham along with the information collected from you and your medical records. The only people in the University of Birmingham who will have access to information that identifies you will be people who need to contact you to 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 or contact details.

The University of Birmingham will keep identifiable information about you from this study for 20 years after the study has finished.

From time to time we may be asked to share the study information (data) we have collected with researchers running other studies in this organisation and in other organisations so that they can perform analysis on the data to answer other important questions about COPD. These organisations may be universities, NHS organisations or companies

involved in health research and may be in this country or abroad. Any such request is carefully considered by the study researchers and will only be granted if the necessary procedures and approvals are in place. 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 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. Under no circumstances will you be identified in any way in any report, presentation or publication arising from this or any other study.

With your permission, we will inform your GP that you are talking part in this research study. We will send your GP a copy of this information sheet.

All individuals who have access to your information have a duty of confidentiality to you.

Involvement of General Practitioner

If you decide to take part in this study, we will contact your GP to let them know

What if something goes wrong?

We do not envisage any problems occurring as a result of your participation in the study. However, all patients are covered for negligent harm according to NHS indemnity guidelines. If you have a concern about any aspect of this study, you should ask to speak to a member of the research team who will do their best to answer your questions <*insert contact number*>. If you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you. Copies of these guidelines are available on request. If you wish to complain about how you have been treated during this study please contact Patient Advice and Liaison Service (PALS) at your local hospital.

Local hospital contact details here:

http://www.doh.gov.uk/patientadviceandliaisonservices/

What if I do not want to take part?

It's up to you to decide whether or not to take part. If you do decide you want to take part you will be given a copy of this information sheet to keep and will be asked to sign a consent form.

You may change your mind about taking part in any aspect of the study at any time (before the start of the study or even after you have commenced the study) for whatever reason without having to justify your decision and without any negative impact on the care you will receive from the medical staff. Exactly what happens if you change your mind depends on which parts of the study you have agreed to and at what point in the study that you change your mind.

Data collected up until withdrawal will be used, anonymously as part of the study outcomes.

What happens if new information becomes available?

Sometimes we get new information about the level of advice being studied. If this happens, a member of the research team will tell you and discuss whether you should continue in the study. You will have the option to decide whether you wish to continue and a member of the research team may ask you to re-sign a consent form if you decide you to continue.

What will happen to the results of the research study?

The results and conclusions will be published in peer reviewed journals, presented at academic meetings and the results of the study will be available via the **Predict&Prevent AECOPD** website.. No individual will be identified in any publication.

Or your local investigator.

Contact Information

If you would like to speak to someone about the study please contact:

< Contact Name > <Job Title>

<Telephone and/or E-mail>

If you would like to gain independent advice relating to study participation you can contact the NHS Patient Advisory and Liaison

Service (PALS)
Tel: *<insert local PALS contact number(s)>* Email: *<insert local PALS email address>*