Effectiveness of **E**lectronic **C**igarettes compared with combination nicotine replacement therapy for smoking cessation in patients with chronic obstructive pulmonary disease **A**nd effect on **L**ung health (ECAL trial)

PARTICIPANT INFORMATION SHEET

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The ECAL trial team would like to invite you to take part in their research trial. Before you decide we would like you to understand why the research is being done and what it would involve for you. Please do take the opportunity to ask any questions.

This information sheet is provided in English. Birmingham Clinical Trials Unit (BCTU) can help with language translation if needed. If you would like access to a translation service, please contact ECAL@trials.bham.ac.uk

What is the purpose of this trial?

Chronic obstructive pulmonary disease (COPD) is a common lung condition which leads to a decline in lung function, and symptoms of breathlessness, cough and/or phlegm that often get worse over time.

About a third of people diagnosed with this condition continue to smoke. It is important that people with COPD who continue to smoke are supported to stop as continued smoking speeds up the progression of the disease and importantly stopping smoking slows it down.

The purpose of this trial is to work out if using an electronic cigarette (vape) can help people with COPD to stop smoking, and how it compares to using nicotine replacement therapy.

As part of the trial, we will also be conducting two additional sub-studies to look at how switching to an e-cigarette affects lung health and wellbeing.

Why have I been chosen?

We are inviting people aged 35 years and older who have been diagnosed with chronic obstructive pulmonary disease (COPD) and are current cigarette smokers to participate in the trial.

What would taking part involve?

To take part in this trial you must want to try to give up cigarette smoking within approximately 2 weeks of starting the trial.

You may have responded to an advert for this trial or received an invitation from your GP practice, local hospital or COPD care team. **If you are interested in taking part** in the trial, we kindly ask that you complete the reply slip and return it to the ECAL trial team following

the instructions on the form. Alternatively, you can express your interest directly to the trial team by sending an email to ECAL@trials.bham.ac.uk or calling 0121 414 3105
You will then be contacted by your local research site or the trial team – see below.

If you are **not a current smoker** or are **not interested** in taking part in this trial, please disregard this invitation.

Please note, there is a reminder invite which will be sent regardless of whether people have, or haven't, completed a reply slip or expressed an interest. If you receive this reminder after returning a reply slip or speaking to the trial team, please ignore it.

What does taking part involve?
Pre-baseline check: If you indicate that you are interested in the trial (by returning the reply slip or expressing an interest to the trial team) you will be contacted over the phone to check you meet the minimum trial entry requirements and, if applicable, set up an appointment for the initial visit. If you have been given this information sheet whilst you are at a participating research site, this pre-baseline check and baseline visit appointment booking may happen face to face at the research site.

Initial visit (baseline): This will be held at your local participating research site and will take roughly 1-2 hours. You will have the opportunity to ask more about the trial and, if you decide to take part, you will be asked to sign a consent form. We will check your medical history, ask you questions about your current health, measure your weight, height and arm span, complete a questionnaire with you, and take a sample of approximately 45ml (2-3 tablespoons) of blood. You will also be asked to complete some simple tests, outlined below:

1. **Spirometry** – you will be asked to blow into a device called a spirometer, which will measure how much air you can blow out and how fast. You may be asked to take a common short acting bronchodilator (e.g. Salbutamol) and then to rest for at least 20 minutes before doing the test.

2. **Exhaled carbon monoxide test -** You will be asked to hold your breath for 15-20 seconds and then blow into a monitor that shows the concentration of carbon monoxide in your breath.

Part of the reason for these tests is to ensure this trial is suitable for you to take part in. If so, you will be allocated at random to one of two treatments which are described below.

- **Treatment arm 1: *Electronic Cigarette (e-cig):*** participants who are assigned to this treatment will receive an e-cig starter pack with an initial supply of e-liquid. You will also receive instructions on how to use the e-cigarette, and where to buy more supplies.

- **Treatment arm 2: *Combination Nicotine Replacement Therapy (NRT):*** Participants who are assigned to this treatment will receive up to 12 weeks supply of nicotine patch and a fast-acting nicotine product (e.g. nicotine gum, lozenge). The type of faster acting product supplied will be dependent on availability and your preference. You will be asked to use a patch and faster acting product for up to 12 weeks.

Calls from a Smoking Cessation Advisor: All participants in the trial will receive phone calls from a trained stop smoking advisor to help them with stopping smoking.

At the first phone call, the advisor will help you to set a target quit date, explain how to use your treatment, and guide in the best approach to stopping smoking. This first call will be shortly after your baseline visit appointment.

They will call you an additional 5 times (on your scheduled target quit day and weekly during the first 4 weeks after your quit day) to provide further help with stopping smoking. Even if you are still smoking, it is important that you participate in these phone calls so we can give you further support and advice and collect important trial data.

Scheduled follow up: All participants will be followed up at the time points below:

- **4 weeks** – During the last behavioural support phone call (approximately 4 weeks after your target quit date) the advisor will complete a questionnaire with you over the phone. If you cannot be contacted by phone, we will send this to you by post to complete and send back.

- **6 months (26 weeks)** – This will involve completing a follow up questionnaire over the phone. If you cannot be contacted by phone, we will send this to you by post to complete and send back.

- **1 year (52 weeks)** - This will be held at your local research site. This appointment will take roughly 1-2 hours. The trained member of the research team will complete a follow up questionnaire with you, measure your weight, take another blood sample and redo the tests outlined above (spirometry and exhaled carbon monoxide test).

Lung health sub-study: You will not need to do anything additional for this sub-study. The data, samples and test results you provide during the ECAL trial might be selected to investigate if there are any differences to lung health between those who vape and other groups such as those who continue to smoke and those who've quit smoking and do not vape. We will be looking at lung health by examining the data we collected from you concerning lung function, symptoms, symptom flare ups (exacerbations), infections and also biomarkers and toxicant levels in the blood.

Wellbeing sub-study: Again, you won't need to do anything additional for this component of the trial. We have incorporated some questions into the questionnaires which will ask how you are feeling during different points of the trial. This data will be looked at to see if there are any differences in anxiety, depression and social quality of life between those who vape and other groups such as those who continue to smoke and those who have quit smoking and do not vape.

Do I have to take part?
No, it is entirely up to you to decide. You will have the opportunity to discuss the trial with a member of the research team.

If you decide to take part, you will be asked to sign a consent form. However, you are free to withdraw at any time and this decision will not affect the care you receive now or in the future. You can withdraw by contacting the ECAL trial team by sending an email to ECAL@trials.bham.ac.uk or calling 0121 414 3105.

If you decide not to take part, this decision will not affect the care you receive now or in the future. Even if you do not want to take part in this trial, the treatments being tested are available either over the counter at most pharmacies or supermarkets/online. Please speak to your GP for further information, or to your local stop smoking service.

How would my treatment group be decided?
The decision regarding which treatment arm you will be allocated to is made randomly by a computer programme at Birmingham Clinical Trials Unit at the University of Birmingham. Like the flip of a coin, you will have an equal chance of being allocated to either treatment. Dividing people in a random way is important because it is the best way to compare treatment fairly.

It is important to remember that everyone who takes part in the trial, whichever treatment they receive, is providing an equally valuable contribution.

What are the possible benefits of taking part?
The treatment you receive might help you to quit smoking. You will also be helping us to improve the treatment and care for people with COPD who want to stop cigarette smoking.

What are the possible disadvantages and risks of taking part?

- You will be asked to provide a blood sample at the initial visit and again a year later. Collecting blood may cause bruising at the place where the needle is inserted.

- All trial products are already in common use in the UK and considered safer than cigarette smoking. Nicotine replacement therapies are licensed medications, and electronic cigarettes/e-liquids are consumer products that are regulated under the Tobacco and Related Products regulation, 2016. Use of nicotine products can result in side effects such as difficulty sleeping (insomnia), sometimes vivid dreams, an upset stomach, dizziness and/or headaches. Some people can get skin irritation when using nicotine skin patches. Some smokers experience throat irritation and cough when they first use e-cigarettes. The side effects are usually mild, but if they are troublesome, please let the smoking cessation advisor know when they call you for your weekly follow up. Alternatively, if the side effects are intolerable, please discontinue use and contact your GP.

Who is organising and funding this trial?
The ECAL trial is being led by Professor David Thickett, Dr Amanda Farley and Dr Aaron Scott and other researchers at the University of Birmingham and at Queen Mary University of London. They are working in partnership with Birmingham Clinical Trials Unit (BCTU) and with patients, GPs and healthcare professional across England, Wales and Scotland. The trial is funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment programme (Ref: NIHR129593) and Efficacy and Mechanisms Evaluation (EME) programme (Ref: NIHR131600).

Have patients and the public been involved in this trial?
A group consisting of patient advisors helped to develop this research study and the research questions that should be asked. This group is also advising the research study team as the study progresses to ensure that the patient's perspective is taken into account as the research is conducted. For example, patient advisors were involved in reviewing this Participant Information Sheet. There is also a patient who is independent of the study team that is a member of a separate committee that oversees the running of the trial, called the Trial Steering Committee.

Who has reviewed the trial?
This trial has been approved by the Medicines and Healthcare products Regulatory Agency (MHRA). All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC), to protect your interests. This trial has been reviewed and given favourable opinion by Newcastle North Tyneside 2 Research Ethics Committee.

Involvement of General Practitioner
You may have been invited through your registered GP practice. Regardless of how you have been invited, we will ask for your permission to inform your GP of your participation in this trial.

In addition, the trial questionnaires ask some questions about your wellbeing. All information given will be held in the strictest confidence however if we have concerns for your well-being, or the wellbeing of others, we have duty of care to inform your GP and/or other health professionals.

What will happen to the samples I give?
Prior to taking any blood, we will require your consent. Any blood samples you provide will be processed at your local research site and some will be frozen and stored at the research site and then transported back to the University of Birmingham labs within the Queen Elizabeth Hospital Birmingham for longer term storage and analysis. We will also ask for your permission to transfer these samples to collaborating organisations and to store any remaining samples after this trial for use in future research which conforms to all relevant legal, governance and ethical requirements.

What if something goes wrong?
In the event that something does go wrong, and you are harmed during the trial there are no special compensation arrangements. If you are harmed, then you may have grounds for legal action, but you may have to pay your legal costs. The University of Birmingham has in place Clinical Trials indemnity coverage for this trial which provides cover to the University for harm which comes about through the University's, or its staff's, negligence in relation to the design or management of the trial. With respect to the conduct of the trial at Site and other clinical care of the patient, responsibility remains with the NHS organisation responsible for the clinical site and is therefore indemnified through NHS Resolution. The University of Birmingham is independent of any pharmaceutical company, and as such it is not covered by the Association of the British Pharmaceutical Industry (ABPI) guidelines for participant compensation. The NHS have a duty of care to participants whether or not the participant is taking part in a clinical trial and the normal NHS complaints mechanisms will still be available to you.

If you have a concern about any aspect of this trial, you should ask to speak to the researchers who will do their best to answer your questions. Please contact the ECAL trial team by sending an email to ECAL@trials.bham.ac.uk or calling 0121 414 3105

If you remain unhappy and wish to complain formally, you can do this by contacting your local Patient Advice and Liaison Service (PALS), which offers confidential advice, support and information. Details can be obtained from: https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

If you have any questions or concerns about taking part in research you can also contact NHS England: Tel: 0300 311 2233, email: england.contactus@nhs.net

Are there any costs to participating?
You will not be paid to take part in the trial. You will be supplied with the trial treatment you have been allocated to free of charge.

You may be reimbursed for any reasonable travel expenses (bus/train/taxi fares) and car park fees for visits related to the trial. These will be paid direct by the trial team, we kindly ask you to keep any relevant supporting documentation of your expenses, such as receipts. You will also be offered a £15 gift voucher, after attending the baseline appointment and the 1 year follow up, to say thank you for your time.

What happens if new information becomes available?
Sometimes we get new information about the treatment being studied. If this happens, a member of the research team will tell you and discuss whether you should continue in the trial. If your research doctor is happy for you to continue in the trial, you will have the option to decide whether you wish to continue. A member of the research team may ask you to re-sign a consent form if you decide you want to continue. If you decide not to carry on, a member of the research team will make arrangements for your standard clinical care to continue. If, however, a member of the research team considers that you should withdraw from the trial, he/she will explain the reasons and arrange for your standard clinical care to continue.

What happens when the research trial stops?
Throughout the trial and once the research trial stops your COPD care will continue as usual. To access support for quitting smoking after the research stops you can contact your local stop smoking service.

What will happen to the results of the research trial?
After the trial has finished and we have reviewed the results, the main findings will be shared with the research sites and GP practices involved in the trial. They will also be available on the ECAL website www.bham.ac.uk/ecal.

The results of this trial will be shared at medical conferences and through publication in academic journals which are read by a large number of health professionals. You will not be individually identified in any poster, report or publication.

How will my personal data be kept secure?
The University of Birmingham and Queen Mary University of London take great care to ensure that personal data is handled, stored and disposed of confidentially and securely. Our staff receive regular data protection training, and the Universities have put in place organisational and technical measures so that personal data is processed in accordance with the data protection principles set out in data protection law.

Any physical paperwork containing identifiable data will be kept in an access-controlled and secured room inside a locked filing cabinet.

In relation to this project, electronic data will be kept on secure, encrypted IT servers within the University of Birmingham and also securely stored on a trusted external database provider, REDCap.

We have a data sharing agreement in place with the central stop smoking service/ pharmacy to ensure we meet accountability obligations under the UK GDPR.

How long will my personal data be kept?
Your data will be retained for up to 25 years after the end of the study at the University for Birmingham. If you withdraw from the project, we will keep the information we have already obtained but, to safeguard your rights, we will use the minimum personally identifiable information possible.

How will we use information about you?
We will need to use information from you and your medical records for this research project. This information will include your NHS number, name, date of birth, contact details, medical history and health information. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

University of Birmingham is the sponsor of this research.

University of Birmingham is responsible for looking after your information. We will share your information related to this research project with the following types of organisations:

- Smoking cessation advisors at Queen Mary's University will have access to your name and contact number(s) to be able to call you for behavioural support and follow up calls. Trained smoking cession advisors will also help us to collect information from you for the trial.

- The central stop smoking service/ pharmacy will have access to you name and address to be able to send you the product you have been allocated.

- If required, we may use a professional interpreter/translator service. This means that an interpreter/translator will be present during our conversation to help translate what is being said. The interpreter/translator is bound by confidentiality

agreements and will not disclose any information discussed during the appointment/call to anyone outside of this conversation.

We will keep all information about you safe and secure by:

- Only allowing approved staff to access to your personal data
- Having procedures in place to deal with any suspected personal data breach
- Writing our reports in a way that no-one can work out that you took part in the trial

International transfers
Your data will not be shared outside the UK.

How will we use information about you after the study ends?
Once we have finished the trial, 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. We will keep your study data for a maximum of 25 years. The study data will then be fully anonymised and securely archived or destroyed.

What are your choices about how your information is used?

- You can stop being part of the trial at any time, without giving a reason, but we will keep information about you that we already have
- You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this
- If you agree to take part in this trial, you will have the option to take part in future research using your data saved from this trial

Where can you find out more about how your information is used?
You can find out more about how we use your information:

- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to dataprotection@contacts.bham.ac.uk, or
- by ringing us on 0121 414 3916

Contact for further information
Please visit our website at www.bham.ac.uk/ecal. If you have any questions, or would like any further information, please contact the ECAL trial team at Birmingham Clinical Trials Unit by sending an email to ECAL@trials.bham.ac.uk or calling 0121 414 3105

If you have any questions or concerns about your healthcare, you can also contact the Patient Advice and Liaison Service (PALS), which offers confidential advice, support and information on https://www.nhs.uk/nhs-services/hospitals/what-is-pals-patient-advice-and-liaison-service/

If you have any queries about the processing of your personal data, please contact dataprotection@contacts.bham.ac.uk for the attention of the Data Protection Officer.

Thank you for taking the time to read this information leaflet and for considering taking part in this trial.

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