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Effectiveness of electronic cigarettes compared with combination nicotine replacement therapy for smoking cessation in patients with chronic obstructive pulmonary disease and effect on lung health (ECAL Trial).

Submission date
03/05/2023

Recruitment status
Recruiting

Registration date
04/10/2023

Overall study status
Ongoing

Last Edited
17/09/2025

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Chronic obstructive pulmonary disease (COPD) is a common lung condition which mainly affects adults aged 35 years and older, and it is most often caused by smoking. COPD symptoms tend to get gradually worse over time and can limit normal activities. Smoking speeds up the progression of COPD but it can be extremely hard to quit, and people with COPD tend to have a greater dependence on nicotine. There are several different treatments available that increase people's chances of successfully quitting smoking; however, many people still relapse back to smoking. Electronic cigarettes (e-cigs) are not currently available on NHS prescription but could help COPD patients to quit smoking. Our goal with this research is to find out how effective e-cigs are compared with combination NRT in helping COPD patients quit smoking cigarettes, and which treatment is more cost-effective for the NHS. The data collected during this trial will also be used to inform a lung health sub-study and wellbeing sub-study. The lung health sub-study will look at the effects of switching to vaping on clinical, physiological and cellular measures of lung health between vapers, continued smokers and quitters. The well-being sub-study will look at the effect of switching to vaping on anxiety, depression and social quality of life compared to those who smoke and quitters.

Who can participate?

People aged 35 years and older who have been identified from selected GP practices and NHS hospitals in England, Wales and Scotland, diagnosed with COPD and are current smokers who want to try to stop smoking

What does the study involve?

This multi-centre trial will invite potentially eligible patients identified from selected GP practices and NHS hospitals in England, Wales and Scotland. Trial participants will be followed up for 1 year. All participants will be asked to have two face-to-face clinic visits to undertake

lung function tests and blood tests. Participants will also receive behaviour support calls from a smoking cessation advisor at set time points through the follow-up period.

What are the possible benefits and risks of participating?
All participants will receive support to stop smoking. There is a potential that participants may be successful in quitting smoking and see an improvement in their health. The products used in this trial are widely used for smoking cessation in standard practice and can be bought over the counter. Participants have no higher risk of side effects than if they were to receive either treatment as part of standard care. The use of nicotine-containing products can result in mild side effects and the main participant information sheet (PIS) advises of these and explains what to do/ who to contact if they experience issues. The participants' GPs will be notified about their participation in the trial, and they will be advised to monitor their patients whilst they try to quit smoking.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
September 2022 to December 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Birmingham Clinical Trials Unit, ECAL@trials.bham.ac.uk (UK)

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1006828

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RG_20-120, IRAS 1006828, CPMS 56604

Study information

Scientific Title
Effectiveness of electronic cigarettes compared with combination nicotine replacement therapy for smoking cessation in patients with chronic obstructive pulmonary disease and effect on lung health (ECAL Trial).

Acronym
ECAL trial

Study objectives
To investigate the effectiveness and cost-effectiveness of Electronic Cigarettes for quitting smoking compared with combination Nicotine Replacement Therapy as an aid to smoking cessation.

To explore change in lung and mental health in people who switch to vaping compared with people who quit smoking without vaping, and people who continue to smoke.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/10/2023, North East - Newcastle & North Tyneside 2 Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8086; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 23/NE/0102

Study design
Multicentre two-arm randomized controlled trial with embedded cost-effectiveness and cohort analyses

Primary study design
Interventional

Study type(s)
Prevention, Efficacy

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Intervention arm: Electronic Cigarettes (EC) - At the baseline visit, participants will be given an EC starter pack and an initial supply of e-liquid (up to 20 mg nicotine/ml). Participants will be provided with instructions on how to continue sourcing further supplies themselves from reputable vendors in their preferred nicotine strength and flavours.

Comparator arm: Combination Nicotine Replacement Therapy (NRT) - Participants will receive up to a 12-week supply of a nicotine patch plus a fast-acting nicotine product to be used in combination. Participants who do not wish to use patches (e.g. due to previous experience with skin irritation) will be offered two types of fast-acting products.

Telephone behavioural support: All participants (intervention and comparator arm) will be advised at the baseline visit that they will receive six weekly behavioural support telephone calls from stop-smoking advisors which will commence within a few days of the baseline visit. During

these calls, the advisor will deliver behavioural support according to the National Centre for Smoking Cessation Training Standard Programme including setting a TQD and providing further support around medication use.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Electronic cigarettes with e-liquid (up to 20 mg nicotine/ml), nicotine patch, fast-acting nicotine product

Primary outcome(s)
Abstinence from smoking since target quit date (TQD) biochemically validated (exhaled CO<8ppm), defined in accordance with the Russell Standard. This will be measured with a questionnaire and exhaled carbon monoxide measurement at 52 weeks post-TQD

Key secondary outcome(s))
1. Abstinence from smoking for at least 26 weeks biochemically validated (exhaled CO<8ppm) measured using a questionnaire at 52 weeks
2. 7-day point prevalence abstinence from smoking biochemically validated (exhaled CO<8ppm) measured using a questionnaire at 52 weeks
3. Self-reported abstinence from smoking for at least 26 weeks measured using a questionnaire at 52 weeks
4. Self-reported 7-day point prevalence abstinence from smoking measured using a questionnaire at 4, 26 and 52 weeks
5. Reduction in cigarettes smoked (self-report of any and > 50% reduction) from baseline to 52 weeks measured using a questionnaire, confirmed by reductions in expired CO readings at 52 weeks
6. Reduction in cigarettes smoked (self-report of any and > 50% reduction) from baseline to 26 /52 week measured using a questionnaire
7. Continued use of the allocated product measured using a questionnaire at 4, 26 and 52 weeks
8. Withdrawal symptoms and urges to smoke (change from baseline to 1/2/3/4 week) measured using the mood and physical symptom scale (MPSS)
9. COPD Symptoms (change from baseline to 4/26/52 week) measured using COPD Assessment Test (CAT) and the Clinical COPD Questionnaire (CCQ)
10. Number of COPD exacerbations over the past 52 weeks (change from baseline to 52 weeks) measured using a questionnaire
11. Number of self-reported upper respiratory tract over the past 52 weeks (change from baseline to 52 weeks) measured using a questionnaire
12. Post bronchodilator spirometry (FEV1, FVC and MMEF change from baseline to 52 weeks). Forced Expiratory Volume in 1 Second (FEV1): The maximal volume of air that can be expired in the first second of a forced expiration from a position of full inspiration (measured in Litres (L) and also expressed as the % predicted for age, sex, height and race). Forced Vital Capacity (FVC): The maximal volume of air that can be expired during a forced and complete expiration from a position of full inspiration (measured in L and % predicted). Mean Mid-Expiratory Flow (MMEF): The average flow between 25% and 75% of the FVC manoeuvre (measured in L/sec and % predicted).

Health economic outcomes:
1. Health-related quality of life (EQ-5D-5L) measured using a questionnaire change from baseline to 4/26/52 weeks
2. Use of healthcare resources and costs measured using a questionnaire at 26 and 52 weeks
3. Cost-effectiveness based on cost per quitter and cost per Quality-Adjusted Life-Year (QALY) at 52 weeks, and modelled cost per QALY over a patient's lifetime

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. COPD diagnosis previously confirmed by post-bronchodilator spirometry (FEV1/FVC <0.7), any GOLD stage
2. Current smoker (≥5 cigarettes per day)
3. Motivated to stop smoking
4. Aged 35 or over

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
35 years

Sex
All

Key exclusion criteria
1. Unable to perform spirometry to a satisfactory standard (e.g. due to dementia, lack of teeth, lack of coordination or not having a good oral seal)
2. Deemed as unsuitable to participate in the trial (e.g. terminal illness, unable to give informed consent)
3. Unable to participate in behaviour support calls
4. Severe angina or unstable cardiovascular disease
5. History of end stage kidney disease
6. History of cirrhosis of the liver
7. Currently taking NRT, bupropion, varenicline or ECs to stop or reduce smoking
8. Currently taking part in another trial of smoking cessation or COPD treatment/management
9. COPD exacerbation or inpatient hospital stay within the last 8 weeks (invite back and re-assess after 8 weeks)
10. Contraindications to spirometry within the last 12 weeks – tuberculosis infection, cardiac infarction, retinal detachment or surgery on the chest, abdomen, brain, ears or eyes (invite back and re-assess after 12 weeks)

Date of first enrolment
26/06/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Gateshead Health NHS Foundation Trust
Queen Elizabeth Hospital
Sheriff Hill
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United Kingdom
NE9 6SX

Study participating centre

The Shrewsbury and Telford Hospital NHS Trust
Mytton Oak Road
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SY3 8XQ

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes