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Exacerbation prevention in patients with both chronic obstructive pulmonary disease and obstructive sleep apnoea

Submission date 06/01/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 20/01/2025	**Overall study status** Ongoing	
Last Edited 10/04/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Patients with chronic obstructive pulmonary disease-obstructive sleep apnoea (COPD-OSA) overlap syndrome have higher rates of COPD exacerbations compared to patients with similar severity COPD without OSA. It is currently unknown whether treating OSA in those with COPD-OSA overlap reduces COPD exacerbation rates. The randomised controlled trial will aim to determine whether giving PAP therapy to patients with COPD-OSA overlap will reduce exacerbations of COPD. Patients with COPD-OSA overlap will be randomised into one of two groups: a) PAP therapy in addition to usual care for COPD compared to b) Usual care for COPD alone.

Who can participate?
Patients with moderate-severe COPD (GOLD grade 2-4), high risk of future exacerbations: 1 severe (hospital assessed) exacerbation or 2 moderate (community clinician assessed) in the last 12 months, and moderate-severe OSA (AHI ≥ 15/h)

What does the study involve?
Participants will be randomised to receive home positive airway pressure (PAP) and COPD usual care or COPD usual care alone with a 12-month follow-up period with an internal pilot.

Usual Care Arm:
If randomised to usual care the following information/advice and management will be delivered: as per NICE (https://www.nice.org.uk/guidance/ng115/resources/chronic-obstructive-pulmonary-disease-in-over-16s-diagnosis-and-management-pdf-66141600098245) and local guidance. This will include as a minimum: a review of pharmacotherapy and consideration of regular, triple-inhaled bronchodilator therapy (long-acting β-agonist, long-acting anti-muscarinic, and steroid), antibiotic prophylaxis, as-needed inhaled short-acting β-agonist therapy, sputum clearance techniques where appropriate, smoking cessation support, pulmonary rehabilitation and education on COPD self-management including non-pharmacological management of COPD, including vaccination additionally advice on sleep quality will be given.

Intervention Arm:
PAP therapy for participants in the intervention arm will be delivered according to local site clinical protocols. All centres involved in the study will be asked for SOPs as part of the process evaluation. Where SOPs are not available senior members of the team will be interviewed to understand the local pathway. As a minimum, the following would be expected for device setup:
1. Face-to-face assessment for mask fitting and device training
2. Mask fit and PAP tolerance check
3. Use of humidification according to patient preference and symptom tolerance
4. Remote review within 1st 30 days to check compliance, troubleshoot technical issues, review mask fit and leak

All participants will undergo face-to-face assessments at 3- and 12-months following randomisation and will complete outcome measures assessments. Trial visits will occur ± 14 days from the scheduled date. Telephone calls will be made monthly (a minimum of 3 attempts will be made over at least three days of the scheduled period of follow-up, after which this the visit will be classed as a missed visit) to collect health care utilisation and PAP therapy (if in the intervention group) data and will be verified at the face-to-face visits.

What are the possible benefits and risks of participating?
Using PAP therapy may reduce participants' risk of having another flare-up of their breathing and improve sleep quality and quality of life. Taking part in the study will help us understand whether PAP therapy is or is not beneficial to patients with COPD and OSA who are at high risk of having repeated exacerbations of their COPD.

All patients taking part in the study will benefit from regular visits with the research team who are experienced in supporting patients with COPD.

There are no expected significant disadvantages to taking part. PAP therapy is used commonly in patients with OSA and severe sleepiness and is tolerated by the majority of patients. However, it can be difficult and uncomfortable for some patients and this is why it is important to understand the potential benefits so patients can make informed decisions on using the treatment. Common side effects are usually minor and include skin discomfort and a runny nose; these may resolve with simple steps, such as additional padding under the mask or a nose spray but also improve over time. If severe they may necessitate stopping PAP and the side effects will then stop. If you do experience any side effects from the machine, please contact your local research team using the telephone numbers on the last page of this leaflet.
Potential risks/side effects of PAP therapy include:
• Skin irritation: the mask can irritate the skin where it is applied. You will be provided with training to fit the mask appropriately to reduce this risk.
• Dry nose, mouth and eyes: The flow of air from the PAP device can sometimes cause drying of the nose, mouth or eyes. This is more common if there is a significant leak from the mask so it will be important to have training to reduce this. Participants will also be offered additional humidification of the air to reduce this problem. Rarely (<5%) nose bleeds can occur following starting PAP.
• Runny nose: It is common when starting PAP therapy to develop a runny nose. This is usually mild and resolves without any treatment but may need treatment with a nasal spray.
• Claustrophobia: Some people can find the mask claustrophobic.
• Swallowing air (called aerophagia): When using the machine, you can sometimes swallow some of the air causing burping or slight discomfort.
All patients receive current “best practice” therapy. All the tests involve little/no discomfort, other than the time taken to perform them. The blowing tests may feel uncomfortable as they require some effort but are safe.

This study will require time and commitment from the patients enrolled, which the research team appreciate and are very grateful for. There are three face-to-face study visits (at the start of the study, 3 months later and at the end of the study at 12 months). These face-to-face visits will take approximately 45 minutes. There are also monthly telephone calls which should take 10 minutes each. All participants will be closely followed up by the research team who are experienced in the management of patients with COPD and OSA.

The study will be under the guidance of a Trial Steering Committee whose job is to ensure that the study is managed well and to monitor safety.
Other potential risks of taking part in the study are felt to be low but could include:
• Distress if you are unable to comply with the PAP treatment or follow-up plans that are part of the trial
• Data risks: Data are collected about participants and their health. These data are collected and stored in line with data protection and clinical trial guidance to reduce the risks but data may be accessed by individuals not directly involved in your care or the trial.

Where is the study run from?
Sponsored by Guys and St Thomas Trust and Trial Management by the University of Oxford, Oxford Respiratory Trials Unit, UK

When is the study starting and how long is it expected to run for?
January 2024 to April 2028

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

Who is the main contact?
Dr Patrick Murphy, Patrick.Murphy@gstt.nhs.uk, epic-osa@ndm.ox.ac.uk

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
332000

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 65205, NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC) Grant Code: NIHR154890

Study information

Scientific Title
Exacerbation prevention in chronic obstructive pulmonary disease (COPD) – obstructive sleep apnoea (OSA) overlap syndrome: The clinical and health economic impact of treating patients with COPD-OSA overlap syndrome and a high risk of future exacerbations with positive airway pressure therapy (PAP) a multicentre randomised controlled trial

Acronym
EPIC-OSA

Study objectives
Patients with chronic obstructive pulmonary disease-obstructive sleep apnoea (COPD-OSA) overlap syndrome have higher rates of COPD exacerbations compared to patients with similar severity COPD without OSA. It is currently not known whether treating OSA in those with COPD-OSA overlap reduces exacerbation rates. COPD exacerbations are characterised by acute transient worsening of symptoms such as dyspnoea, sputum production, sputum purulence and cough which are above the normal day to day variation in symptom burden and are usually associated with escalation of medical therapy. Exacerbations are significant events impacting on patient's quality of life, lung function, future exacerbation risk and survival. Exacerbations are recognised as a significant concern by patients, with exacerbation prevention ranked as the number one research priority by COPD patients. The study aims to determine whether giving PAP (positive airway pressure) therapy to patients with COPD-OSA overlap will reduce exacerbations of COPD. A randomised controlled trial will be undertaken, patients with COPD-OSA overlap will be randomised to one of two groups: a) PAP therapy in addition to usual care for COPD, b) usual care for COPD alone.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 24/12/2024, London - Westminster Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8066; westminster.rec@hra.nhs.uk), ref: 24/LO/0818

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Respiratory

Interventions
This is a multi-centre randomised controlled trial in patients with COPD-OSA overlap and a high risk of exacerbations. Participants will be randomised via a web-based, pre-programmed

randomisation system with minimisation for Epworth sleepiness score (<11 or ≥11), current long-term oxygen therapy use (Y/N) and study site, to receive home PAP and usual COPD care or usual COPD care alone with a 12-month follow-up period.

Several methods will be used to identify patients. Patients will be identified by clinical teams when attending clinical review in COPD clinics, rehabilitation services or sleep clinics. Where appropriate, patients who have attended community diagnostic centres for spirometry and have results consistent with COPD will be screened. Lastly, where possible local screening databases will be used to identify additional patients with COPD. Where possible clinical teams will be asked to record STOP-BANG and Epworth Sleepiness Score (ESS), if this is not feasible at the clinical visit, this will be done at screening. If patients meet the inclusion requirement they will be asked to consent to the study and undergo a sleep study. Following the sleep study patients with moderate to severe OSA will be randomised to PAP therapy or usual care.

At baseline assessment (visit 1) medical history, drug history and COPD clinical history will be recorded. Participants will also be asked to complete questionnaires including CAT, EQ-5D-5L, eMRCD score, Pittsburgh sleep quality index and Epworth Sleepiness Score. Spirometry (lung function testing will also be undertaken.
Participants will then be reviewed at 3 and 12 months and all of the assessments in the baseline visit are repeated. In addition, PAP usage data will be recorded as well and any support for PAP therapy will be given.

Participants will also be contacted every month to:
1. Record health care utilisation
2. Exacerbations (number and treatment given)
3. Medication changes
4. Use of PAP therapy and if any support is required with this
5. Record any adverse or serious adverse events
6. Participants will also be asked to complete questionnaires including CAT, EQ-5D-5L, eMRCD score

Intervention Type
Procedure/Surgery

Primary outcome(s)
Exacerbation frequency measured using exacerbation frequency 12 months post-randomisation data collected by the hospital, community and self-treated at randomisation, baseline to 12 months

Key secondary outcome(s))
Secondary outcome measures
1. The impact of 12 months of PAP therapy on quality of Life measured using the Chronic Obstructive Pulmonary Disease Assessment Test (CAT) score, extended MRC-Dyspnoea (eMRCD) score and 5-level EQ-5D version (EQ-5D-5L) at randomisation, baseline and 12 months
2. The impact of 12 months of PAP therapy on patient-reported sleep quality and daytime sleepiness measured using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Score (ESS) at randomisation, baseline and 3 and 12 months
3. The impact of 12 months of PAP therapy on Lung Function measured using Spirometry at randomisation, baseline and 3 and 12 months
6. The dose-response relationship between hours of PAP use and primary and secondary outcomes measured using usage hours downloaded from the PAP device, exacerbation

frequency, patient-reported questionnaires (CAT, EQ5D5L, eMRCD, ESS, PSQI), spirometry, and healthcare utilisation at randomisation, baseline and 3 and 12 months (intervention group only)
7. The cost-effectiveness of PAP treatment in patients with COPD-OSA overlap in the UK health system over 12 months measured using data collected regarding healthcare utilisation and EQ5D5L at randomisation, baseline and 12 months

Exploratory
To explore the relationship between primary outcome and health-related quality of life based on COPD clinical phenotypes the following outcome variables will be assessed using participant characteristics, primary and secondary outcomes (exacerbation frequency, patient-reported questionnaires (CAT, EQ5D5L, eMRCD, ESS, PSQI), spirometry, healthcare utilisation) at randomisation, baseline and 12 months:
1. Significant sleepiness (defined as an ESS>/= 11),
2. Poor Sleep quality (defined as PSQI >5)
3. GOLD ABE grouping
4. Eosinophilic COPD (yes/no)
5. Bronchitic COPD (yes/no)

Completion date
13/04/2028

Eligibility

Key inclusion criteria
1. Moderate-severe COPD (GOLD grade 2-4)
2. High risk of future exacerbations: 1 severe (hospital assessed) exacerbation or 2 moderate (community clinician assessed) in the last 12 months
3. Moderate-severe OSA (AHI ≥ = 15/h)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Clinically significant or severe daytime sleepiness: Epworth Sleepiness score > 15 or excessive sleepiness likely to impair safe driving in current drivers (as evidence has already established that such patients should be treated with PAP therapy)
2. Significant hypercapnic respiratory failure at baseline assessment ($PaCO_2$ > 6kPa, with evidence already indicating these patients should be treated with NIV)
3. PAP therapy mandated by the treating clinician due to the severity of the sleep symptom burden
4. Professional driver or other vigilance essential role with significant daytime sleepiness
5. Currently enrolled in an interventional clinical trial

Date of first enrolment
01/03/2025

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Thomas' Hospital (Leading sponsor site)
Guy's and St Thomas' NHS foundation trust
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Royal Free Hospital
Royal Free London NHS Foundation Trust
Pond Street
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NW3 2QG

Study participating centre
Freeman Hospital
Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Road
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United Kingdom
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Study participating centre
John Radcliffe Hospital
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OX3 9DU

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Sponsor information

Organisation
Guy's and St Thomas' NHS Foundation Trust

ROR
https://ror.org/00j161312

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
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet version 1.0	11/11/2025	11/11/2025	No	Yes
Protocol file		14/10/2024	13/01/2025	No	No