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What is the clinical effectiveness and cost-effectiveness of nebulised 7% sodium chloride in patients with chronic obstructive pulmonary disease?

Submission date
03/03/2021

Recruitment status
No longer recruiting

Registration date
01/06/2021

Overall study status
Completed

Last Edited
18/11/2025

Condition category
Respiratory

[_] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory lung disease that causes obstructed airflow from the lungs. Symptoms include breathing difficulty, cough, mucus (sputum) production and wheezing.
We want to study whether breathing in salty water through a nebuliser can help patients with COPD cough up phlegm, make them feel better and cut down the number of chest infections they have. We also would like to know whether this is better than taking capsules (carbocisteine), also thought to help patients clear phlegm from the airways.
A nebuliser is a machine that creates a mist, which can be inhaled through a mask or tube. The salty water can be inhaled through a nebuliser to help clear excess mucus from the airways. There is poor evidence of what treatments help clear mucus from the airways. Usually carbocisteine tablets are used (to help clear mucus from the airways). The study investigators believe inhaling salty water is better at clearing mucus from the airways and has additional beneficial effects combating bacterial and viral infection.

Who can participate?
Participants aged 18 years or older with COPD that have either chronic bronchitis and/or associated bronchiectasis and have self-reported difficulty self-expectorating

What does the study involve?
We will recruit 860 patients with COPD throughout the UK.
Half of the group, at random, will inhale salty water through a nebuliser twice a day for 1 year. The other half will get carbocisteine capsules daily for 1 year. It is not possible for it to be a blind trial because the participants and clinician will obviously know the treatment given. Both groups will be taught chest clearance using a video of breathing and coughing techniques that they can use twice a day to help clear phlegm from the chest.
The main goal of the study is to see whether inhaled sodium chloride is better and is more cost-effective than oral carbocisteine which is the traditional medication used. Theoretically, inhaled

sodium chloride is better than carbocisteine at clearing phlegm in the airways.
Participants will be asked to attend three appointments in total – one to join the study and again at 6 months and 1 year.

What are the possible benefits and risks of participating?
There are no direct benefits to taking part in this study, but the results from this study might help to improve the healthcare of patients in the future.
There are not thought to be many disadvantages to taking part in the study. It does involve taking time to attend three appointments and undergo tests, complete diaries each week for a year and complete three questionnaires which might not find convenient.
Some patients may experience side effects from taking the study medications. Like with any new medication there is a risk of allergic reaction.

Where is the study run from?
NHS Lothian (UK)

When is the study starting and how long is it expected to run for?
June 2020 to November 2024

Who is funding the study?
The NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
1. Beatrice Selby, bselby@ed.ac.uk
2. Prof. Adam Hill, adam.hill@nhs.scot

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-001949-39

Integrated Research Application System (IRAS)
281629

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AC20047, HTA - NIHR128443, IRAS 281629

Study information

Scientific Title
An open pragmatic UK multi-centre parallel randomised controlled trial with process evaluation and health economic analysis in participants with COPD that have either chronic bronchitis and/or associated bronchiectasis that have self-reported difficulty self-expectorating to assess whether nebulised 7% sodium chloride plus Active Cycle Breathing Technique (ACBT) is superior compared with carbocisteine plus ACBT when comparing the change in COPD Assessment Tests (CAT) over one year period.

Acronym
MucAct COPD

Study objectives
This study will provide knowledge on whether hypertonic sodium chloride is superior to carbocisteine in aiding sputum expectoration. In addition to improving sputum clearance, it is expected that there will be a prolongation in time to first exacerbation and overall a reduced number of exacerbations over one year.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 09/04/2021, East Midlands - Leicester South Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44(0)207 1048310; leicestersouth.rec@hra.nhs.uk), ref: 21/EM/0074

Study design
Open pragmatic UK multi-centre parallel randomized controlled trial with process evaluation and health economic analysis

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Participants with Chronic Obstructive Pulmonary Disease that have either chronic bronchitis and /or associated bronchiectasis that have self-reported difficulty self-expectorating

Interventions
Participants will be randomised on a 1:1 basis to nebulised 7% sodium chloride plus ACBT or 750mg carbocisteine plus ACBT.
The randomisation system will include allocation concealment and stratification for current smoking status, COPD severity (GOLD class 1 and 2 versus 3 and 4).

The active arm will receive twice daily nebulised 7% sodium chloride + self-administered ACBT chest clearance. The participants are self-administering nebulised 7% sodium chloride and will be allowed to increase the frequency of use up to a maximum of 6 times per day during respiratory tract infections (minimum four times daily where possible).

Participants allocated to the nebulised 7% sodium chloride arm will be instructed to administer a 1 x 4 mL ampoule twice daily for 52 weeks using the nebuliser provided by their local study team. Nebulisation takes less than 10 minutes.

Some patients have bronchospasm with nebulised 7% sodium chloride. If these symptoms develop, treatment with nebulised 2.5mg salbutamol is recommended prior to taking the nebulised 7% sodium chloride. Nebulised 2.5mg salbutamol can also be used post hypertonic sodium chloride if needed.

The comparator arm with carbocisteine will receive oral carbocisteine (750 mg of carbocisteine three times per day for 8 weeks, reducing to 750 mg twice per day over 44 weeks) + self-administered ACBT chest clearance. The dose of carbocisteine is in accordance with the British National Formula (BNF).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)

Nebulised sodium chloride, carbocisteine

Primary outcome(s)
Impact of COPD measured using the COPD Assessment Test (CAT) at baseline and one year

Key secondary outcome(s))
1. Health related quality of life:
1.1. CAT score at baseline and 6 months
1.2. Quality of life assessment using the Leicester Cough Questionnaire and St. George's Respiratory Questionnaire at 6 months and 1 year
2. Exacerbations and time to first exacerbation:
2.1. Number of exacerbations over a one year period requiring antibiotic therapy and/or systemic steroid treatment measured using exacerbation diaries when exacerbation is reported by the patient
2.2. Time to first exacerbation requiring antibiotic therapy and/or systemic steroids over one year measured using exacerbation diaries when exacerbation is reported by the participant
2.3. Proportion of exacerbations needing antibiotic therapy over one year measured using exacerbation diaries when exacerbation is reported by the patient and concomitant medication recording
2.4. Number of upper respiratory tract infections (URTI) over a one year period) assessed using the Wisconsin Upper Respiratory Symptom Survey-24 (WURSS-24)
2.5. Overall and COPD related hospital attendances/admissions over one year measured using healthcare usage questionnaire at baseline, 6 months and 12 months
2.6. Use of nebulised 7% sodium chloride in exacerbations measured using participant reported daily diaries
3. Potential pathogen microorganisms and viruses from sputum samples and combined nose and throat swabs:
3.1. Proportion being infected with a potential pathogenic organism and viruses at 6 months and one year (from sputum samples and combined nose and throat swabs (if taken as part of standard care))
4. Viral transmissibility (household contacts to participant and participant to household contacts) measured using participant reported daily diaries
5. Lung function:
5.1. Forced Expired Volume in 1 second (FEV1), forced vital capacity (FVC) and mid-expiratory flows at 6 months and one year
6. Health economic benefits:
6.1. Cost per Quality Adjusted Life Year (QALY) a) over one year and b) modelled over a lifetime horizon measured using healthcare usage questionnaire at baseline, 6 months and 12 months
7. Adverse effects over one year measured using participant reported daily diaries
8. Adherence with interventions assessed by weekly participant charts and enquired at study appointments over one year

Completion date
14/11/2024

Eligibility

Key inclusion criteria
1. Patients ≥18 years old
2. Have COPD as the predominant respiratory diagnosis
3. Meet Medical Research Council (MRC) definition of chronic bronchitis, defined

epidemiologically as cough and sputum production for ≥3 months per year in at least 2 consecutive years and/or have associated bronchiectasis on computed tomography of the chest
4. Self-reported difficulty in expectoration (determined from the medical notes and/or participant). If from the participant, this will be documented in the medical notes

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
206

Key exclusion criteria
Current participant exclusion criteria as of 16/12/2022:
1. Patients that do not have the capacity to consent (determined by clinician or member of the research team)
2. Patients with active malignancy
3. Patients with a solid organ transplant
4. Patients with active tuberculosis
5. Patients who are in end-of-life care
6. Patients who have had treatment with nebulised hypertonic sodium chloride, carbocisteine or any muco-active treatments within the past 7 days*
7. Patients who are established on long-term antibiotic therapy for less than 3 months
8. Patients who have had an exacerbation within the past 14 days requiring treatment with antibiotics and/or steroids**
9. Known contraindication or intolerance to nebulised 7% sodium chloride or carbocisteine or any hypersensitivity to the active ingredients or the excipients of carbocisteine
10. Active peptic ulceration; any known hereditary galactose intolerance, Lapp-Lactase deficiency or glucose-galactose malabsorption
11. Women who are pregnant or currently breastfeeding
12. Women of childbearing potential*** not taking appropriate contraception****. Contraception must be continued for a minimum of 30 days after the end of the IMP dosing schedule.
13. Participation in another Clinical Trial of an Investigational Medicinal Product (CTIMP) within the last 30 days
14. Previous recruitment to the study
15. Participants indicating that they are unable to comply with the study protocol prior to

randomisation including those unable to complete participant questionnaires
*If participants have been on treatment with nebulised 7% sodium chloride, carbocisteine or any muco-active treatments within the past 7 days, they need to come off these treatments for 7 days and remain clinically stable in order to be eligible for the study
**14 days from the start of the recent exacerbation
*** A woman is considered of childbearing potential (WOCBP), i.e. fertile, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormone replacement therapy. However, in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
****Acceptable contraception in women of childbearing age is a “highly effective” contraceptive measure as defined by the Clinical Trials Facilitation Group and includes combined (oestrogen and progesterone containing) or progesterone-only contraception associated with inhibition of ovulation, or intrauterine device or bilateral tubal occlusion (http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2014_09_HMA_CTFG_Contraception.pdf).

Previous participant exclusion criteria:
1. Patients that do not have capacity to consent (determined by clinician or member of the research team)
2. Patients with an active malignancy
3. Patients with a solid organ transplant
4. Patients with active tuberculosis
5. Patients who are in end-of-life care
6. Patients who have had treatment with nebulised hypertonic sodium chloride, carbocisteine or any muco-active treatments within the past 30 days*
7. Patients established on long-term antibiotic therapy for less than 3 months
8. Patients who have had an exacerbation within the past 30 days requiring treatment with antibiotics and/or steroids
9. Known contraindication or intolerance to nebulised 7% sodium chloride or carbocisteine or any hypersensitivity to the active ingredients or the excipients of carbocisteine
10. Active peptic ulceration; any known hereditary galactose intolerance, Lapp-Lactase deficiency or glucose galactose malabsorption; patients unable to swallow oral capsules
11. Women who are pregnant or currently breastfeeding
12. Women of childbearing potential** not taking appropriate contraception***. Contraception must be continued for a minimum of 30 days after the end of the IMP dosing schedule
13. Participation in another Clinical Trial of an Investigational Medicinal Product (CTIMP) within the last 30 days
14. Previous recruitment to the study
15. Participants indicating that they are unable to comply with the study protocol prior to randomisation including those unable to complete participant questionnaires

*If participants have been on treatment with nebulised 7% sodium chloride, carbocisteine or any muco-active treatments within the past 30 days, they need to come off these treatments for 30 days and remain clinically stable in order to be eligible for the study.
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stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post-menopausal state in women not using hormonal contraception or hormonal replacement therapy. However in the absence of 12 months of amenorrhea, a single FSH measurement is insufficient.
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Date of first enrolment
01/05/2021

Date of final enrolment
01/12/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Royal Infirmary of Edinburgh
NHS Lothian
51 Little France Crescent
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Scotland
EH16 4SA

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon and Exeter NHS Foundation Trust
Barrack Road
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EX2 5DW

Study participating centre
Glasgow Royal Infirmary
NHS Greater Glasgow and Clyde

1055 Great Western Road
Glasgow
Scotland
G4 0SF

Study participating centre
University Hospital Wishaw
NHS Lanarkshire
50 Netherton Street
Wishaw
Scotland
ML2 0DP

Study participating centre
Freeman Hospital
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Road
Newcastle-upon-tyne
England
NE7 7DN

Study participating centre
Bradford Royal Infirmary
Bradford Teaching Hospitals NHS Foundation Trust
Duckworth Lane
Bradford
England
BD9 6RJ

Study participating centre
Royal United Hospital
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
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BA1 3NG

Study participating centre
Gloucestershire Royal Hospital
Gloucestershire Hospitals NHS Foundation Trust
Great Western Road

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GL1 3NN

Study participating centre
Raigmore Hospital
Old Perth Rd
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Study participating centre
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Bordesley Green East
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Study participating centre
Birmingham Good Hope Hospital
Rectory Road
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Study participating centre
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BR6 8ND

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WS2 9PS

Study participating centre
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Foresterhill Road
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AB25 2ZN

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Study participating centre
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Kirkcaldy
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Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

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?

Basic results		12/11/2025	18/11/2025	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 4	09/08/2022	13/08/2025	No	No
Protocol file	version 5.0	01/05/2023	28/10/2025	No	No
Statistical Analysis Plan	version 1.0	22/05/2025	18/11/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes