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Sputum colour charts to guide antibiotic self-treatment of acute exacerbation of COPD

Submission date	**Recruitment status**	[X] Prospectively registered
10/11/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/11/2020	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
12/12/2024	Respiratory	

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a long-term condition affecting 2 million people in the UK, causing over 140,000 hospital admissions and 1.7% of UK hospital bed days per year. Common day-to-day symptoms include breathlessness, which is typically worse on exertion, and a cough that produces sputum (phlegm or mucus). One approach to reduce the impact of exacerbations (worsening of COPD symptoms) is the use of self-management (SM) plans, alongside a pack of antibiotics and steroids. The main aim of this study is to assess the effectiveness of using sputum colour charts alongside a self-management SM plan to guide antibiotic self-treatment by patients with acute exacerbations of COPD (AECOPD).

Who can participate?
Patients aged 18 and over with COPD who have had two or more AECOPDs in the previous 12 months OR one or more hospital admissions related to COPD.

What does the study involve?
Participants may be given a sputum colour chart in addition to the usual standard advice. This is a card with different colours on it that covers the range of colours of sputum that they may produce. The researchers are assessing whether the use of this colour chart will help patients manage their symptoms safely and more effectively than just having the standard advice. Participants will be randomly allocated to either have the self-management plan alone or the self-management plan with the sputum colour chart. All patients who take part in the study (regardless of group allocation) will receive two appointments: one at the start and one at the end of the study (12 months). These appointments will be similar to the annual COPD review and will be with the nurse providing the patient's usual care. Appointments will take place over the telephone, via a video link or face-to-face at their GP practice. Patients will also receive telephone calls at 2 weeks and at 3, 6 and 9 months after they enrol on the study. During these calls they will be asked questions regarding their symptoms so that the researchers can record details of any COPD exacerbations which they may have had since agreeing to participate in the study. The questionnaires have been carefully designed with the help of patients and the public to cause as little burden as possible whilst still collecting the information the study needs, but they are in addition to usual care.

What are the possible benefits and risks of participating?
This study will help us to find out which level of support is better at helping patients manage their symptoms. There may be no immediate benefits to taking part, but the aim in the longer term will be to improve care for patients with COPD. The researchers do not know if having extra information will help patients better manage their illness or not. They hope to find this out by doing this study. They could find that having more information makes patients less sure about how to manage their illness, but patients will be closely monitored by the research team throughout the study and any queries and concerns will be dealt with as they arise.

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

When is the study starting and how long is it expected to run for?
December 2019 to March 2024

Who is funding the study?
National Institute of Health Research, Health Technology Assessment (NIHR HTA) (UK)

Who is the main contact?
colourcopd@trials.bham.ac.uk

Study website
https://www.birmingham.ac.uk/ColourCOPD

Contact information

Type(s)
Public

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
263204

ClinicalTrials.gov number
NCT04705233

Secondary identifying numbers
CPMS 42074, IRAS 263204

Study information

Scientific Title
A two-arm, multi-centre, open-label, parallel-group randomized designed trial investigating the use of sputum colour charts to guide antibiotic self-treatment of acute exacerbation of COPD in patients with COPD (Colour COPD)

Acronym
Colour COPD

Study objectives
This study is a pragmatic, individually randomized trial, set in primary care, comparing usual care to the use of a sputum colour chart in patients at risk of hospital admission for AECOPD, with the hypothesis that use of a colour chart will be non-inferior to usual care with respect to hospital admission rate after 12 months of follow-up, this being the primary outcome measure.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/11/2020, Yorkshire & The Humber - South Yorkshire Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 1048091; southyorks.rec@hra.nhs.uk), REC ref: 20/YH/0273

Study design

Randomized; Both; Design type: Treatment, Education or Self-Management, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Will be available on the study website (not yet active)

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

Interventions
With the support of the Clinical Research Network, potential participants will be identified by pre-screening of GP records and patients will be sent a Patient Information Sheet (PIS) by post to give further information about the trial. Once adequate time has been allowed to consider the study, a screening appointment (appointment 1) will be undertaken by a Healthcare professional (a Nurse/Research nurse).

For Appointment 1 (screening) and Appointment 2 (12-month follow up) one of the following four delivery methods will be used (in order of preference, and to cover all eventualities):
1. Face to face
2. Video consultation
3. Telephone with video links sent via email to all parties to assist with the delivery of the intervention i.e. instructions on how to use the SM Plan +/- sputum colour chart
4. Telephone only (with written instructions posted to intervention participants)

Appointment 1:
The study will be explained and informed consent will be taken prior to any study assessments being conducted. This initial appointment will be similar to the normal annual COPD review and therefore aligns well with usual care. After the patient has been assessed against the inclusion /exclusion criteria the following activities will take place:
1. Patient demographics and education level recorded
2. A review of medical history and concomitant medication
3. Smoking status confirmed
4. Quality of life questionnaires (CAT and EQ-5D-5L) completed (the nurse to ask the patient the questions and record their answers)
5. MRC score (perceived breathlessness scale) to be determined and recorded
5. Randomisation (via a computerised system) to either the intervention or usual care arm of the study.
6. Record lung function measurements from existing medical history
7. Assess whether the patient has chronic bronchitis

Telephone calls:
A telephone call will be made by the central research team to the patient 2 weeks after appointment 1 to assess intervention fidelity and provide technical support for e-diary app users (where applicable). Telephone calls will also be made 3 months, 6 months and 9 months after Appointment 1. At each timepoint the patient will be asked if they are happy to reconfirm consent to continue with the study and information regarding any acute exacerbations of COPD since their last study contact will be recorded. Adverse events (defined as any untoward medical occurrence) will also be recorded. The CAT and EQ-5D-5L questionnaires will be completed by reading the questions to the patient and recording their responses.

Appointment 2
This will take place 12 months after enrolment (12 months post-randomisation) and as with Appointment 1, it will be similar to the normal annual COPD review. Following reconfirming consent, CAT and EQ-5D-5L questionnaires will be completed. Smoking status and concomitant medication will be recorded, together with MRC score and lung function measurements FEV1 and FVC. Information regarding any acute exacerbations of COPD since last study contact will be collected and recorded. Adverse events will also be recorded. Data will also be collected from the existing GP record. Outcomes such as hospitalisations and mortality will be collected from HES as well as the existing medical record with the merged data being taken to represent the total number of medically confirmed exacerbations. Self-reported AECOPD will be compared to that confirmed in the medical record, however, the medically confirmed value will be assumed as the true number for the purpose of our secondary outcome analysis of AECOPD rate and subsequent economic evaluation. A specific Case Report Form (CRF) will be used to collect all study data and outcomes.

E-diary sub-study:
Patients will be approached about this sub-study at Appointment 1 and if eligible and consent is obtained they will be given access to the e-diary via an app on their mobile device or tablet. A demonstration of the app will be given using instruction materials provided by the e-diary provider. A written copy of these materials will also be given to patients to take away. Where appointments take place remotely (over the telephone or video link) participants will be talked through how to set up and use the app and written instructions will be sent to them via email or post. They will be asked to complete the e-diary on a daily basis and will receive a telephone call from the central research team 2 weeks after enrolment into the study during the 2-week phone call and they will be encouraged to use the diary if they are not actively doing so by that point and technical support will be provided if required. Site staff will be alerted if the completion drops below 50% of days in any given month and the patient will be contacted to check the reason for non-completion and address any issues.

Sputum sub-study:
Those patients who have chronic bronchitis will be approached at Appointment 1 for the sputum sub-study. If they consent to this they will be provided with five sputum pots and materials to post the samples to the lab, together with an instruction leaflet detailing how and when to send samples. Samples will be requested at the start and end of the study, and also at all AECOPD, with sputum pots being replenished via their usual care provider as required. Sputum samples will be processed centrally at the lab at the University of Birmingham, and data transferred securely to the trials unit regularly, or immediately if a pathogen is present and may require clinical action. The research team will contact patients with any positive or negative results by their chosen communication method (e.g. telephone or email). The patient's GP will also be informed of any positive sputum infection results. Data will be collected on sputum colour as

determined by the laboratory staff against the Bronkotest® chart, pathogens present, and the number of colony-forming units/ml of each potential pathogen seen, as well as any antibiotic resistance seen on routine sensitivity testing.

Qualitative sub-study:
Some patients and healthcare staff (nurses and doctors) will be approached about participating in research interviews to explore their experiences of living with COPD/managing patients with COPD. These interviews will also ask patients and healthcare staff about their experiences of participating in the main COPD Trial and use of the colour sputum colour charts.

Intervention Type
Other

Primary outcome measure
A binary outcome assessing the incidence of at least one AECOPD over 12 months post randomisation where patients needed hospitalisation (defined by hospital discharge letter /coding). Data will be obtained from NHS digital medical records (hospital episode statistics; HES) which ensures any admissions not reported to the GP are picked up.

Secondary outcome measures
Current secondary outcome measures as of 16/02/2021:

1. Number of self-reported AECOPD every 3 months. Time Frame: 3, 6, 9 and 12 months post randomisation
2. Number of self-reported antibiotic and steroid prescriptions for AECOPD. Time Frame: 3, 6, 9 and 12 months post randomisation
3. Number of all cause hospital admissions. Time Frame: 12 months post randomisation taken from Hospital Episode Statistics (HES) and/or participant self-report
4. Number of readmissions to hospital for AECOPD at 30 and 90 days. Time Frame: 12 months post randomisation taken from HES and/or participant self-report
5. Number of Bed days due to AECOPD. Time Frame: 12 months post randomisation taken from HES and/or participant self-report
6. Number of participant deaths from all causes. Time Frame: 12 months post randomisation. All-cause mortality taken from HES and/or medical records
7. Number of unscheduled GP visits for AECOPD. Time Frame: 12 months post randomisation
8. Number of prescriptions for 2nd courses of antibiotics within 14 days of self-reported event (defined as treatment failure). Time Frame: 12 months post randomisation
9. Number of prescriptions for oral anti-fungals. Time Frame: 12 months post randomisation
10. Quality of life by COPD assessment test. Time Frame: 3, 6, 9 and 12 months post randomisation
11. Quality of life measured using the COPD assessment test (CAT) at 3 monthly intervals
12. Quality of life measured using the EuroQoL-5Dimension-5Level (EQ-5D-5L) questionnaire. Time Frame: 3, 6, 9 and 12 months post randomisation
13. Antibiotic resistance. Time Frame: at baseline, all AECOPD and 12 months post randomisation
14. Healthcare resource utilisation. Time Frame: 3, 6 and 9 and 12 months post randomisation. Determined from participant self-report on bespoke questionnaire

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Previous secondary outcome measures:

1. Self-reported AECOPD (including those for which admission is required) obtained by telephone calls to patients at 3, 6 and 9 months
2. GP-confirmed antibiotic and steroid prescriptions for AECOPD at 12 months
3. All-cause hospital admission taken from HES and/or medical records and measured at 12 months
4. Readmissions to hospital for AECOPD at 30 and 90 days taken from HES and/or medical records at 12 months
5. Bed days due to AECOPD taken from HES and/or medical records at 12 months
6. All-cause mortality taken from HES and/or medical records at 12 months
7. Unscheduled GP visits for AECOPD taken from medical records at 12 months
8. Prescriptions for 2nd courses of antibiotics within 14 days of self-reported event taken from medical records at 12 months
9. Prescriptions for oral anti-fungals taken from medical records at 12 months
10. Quality of life measured using COPD assessment test (CAT) and EQ-5D-5L at 3, 6 and 9 months
11. Antibiotic resistance measured by sputum culture at baseline, all AECOPD and 12 months
12. Healthcare resource utilisation determined from healthcare records at 12 months and patient at 3, 6 and 9 months

Overall study start date
01/12/2019

Completion date
30/03/2024

Eligibility

Key inclusion criteria
1. Clinically diagnosed COPD, confirmed by a medical record of post-bronchodilator spirometry denoting obstruction
2. ≥2 AECOPD in the 12 months prior to screening according to the patient OR ≥1 hospital admission for AECOPD (i.e., GOLD C or D)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 2954; UK Sample Size: 2954

Total final enrolment
115

Key exclusion criteria
Household member already participating in the study

Date of first enrolment
30/11/2020

Date of final enrolment
30/03/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
CRN West Midlands
Birmingham Research Park
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B15 2SQ

Study participating centre
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Nelson Street
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M13 9NQ

Study participating centre
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Study participating centre
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M14 6WP

Study participating centre
Brierley Park Medical Centre
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NG17 2NF

Study participating centre
Chilwell Valley and Meadows Practice
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Study participating centre
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Study participating centre
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Edgbaston
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United Kingdom
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Study participating centre

Windrush Medical Practice
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Witney
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OX28 6JS

Study participating centre
Woodgate Valley Health Centre
61 Stevens Avenue
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Birmingham
United Kingdom
B32 3SD

Study participating centre
White Horse Medical Practice
Faringdon Medical Centre
Volunteer Way
Faringdon, Oxfordshire
United Kingdom
SN7 7YU

Study participating centre
Brownlow Health @ Princes Park
Princes Park Health Centre
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Toxteth
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Study participating centre
Church Street Practice
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United Kingdom
OX12 9BN

Study participating centre
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299 Bordesley Green East

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Birmingham
United Kingdom
B33 8TA

Sponsor information

Organisation
University of Birmingham

Sponsor details
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Sponsor type
University/education

Website
http://www.birmingham.ac.uk/index.aspx

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 17/128/04

Results and Publications

Publication and dissemination plan

Documents will be available on the study website (not yet active). Dissemination will occur through conferences and publications, as well as through our PPI group and newsletter. Impact is anticipated through updates to UK COPD guidance around SM plans for AECOPD. The researchers plan to publish the results of the trial in a high-impact peer-reviewed journal. A summary of the results will also be available on the study website (https://www.birmingham.ac.uk/colourcopd).

Intention to publish date
30/06/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from BCTU (bctudatashare@contacts.bham.ac.uk). Data will typically be available within 6 months after the primary publication unless it is not possible to share the data (for example the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data). Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the Chief Investigator and, where appropriate (or in absence of the Chief Investigator) any of the following: the Trial Sponsor, the relevant Trial Management Group (TMG), and the independent Trial Steering Committee (TSC). A formal Data Sharing Agreement (DSA) may be required between respective organisations once the release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers the transfer of patient identifiable information. Any data transfer will use a secure and encrypted method.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	mixed methods substudy establishing the prevalence of CVD in primary care,	04/03/2021	03/12/2021	Yes	No
Protocol file	version 6.0	03/10/2022	02/02/2023	No	No
HRA research summary			28/06/2023	No	No
Results article		07/11/2024	12/12/2024	Yes	No