ISRCTN24346473 https://doi.org/10.1186/ISRCTN24346473

Primary care use of a C-Reactive Protein (CRP) Point of Care Test (POCT) to help target antibiotic prescribing to patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) who are most likely to benefit

Submission date 13/08/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/08/2014	**Overall study status** Completed	
Last Edited 03/12/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

Chronic obstructive pulmonary disease (COPD) is a group of lung conditions that cause breathing difficulties. People with COPD often experience sudden worsening of symptoms, known as acute exacerbations of COPD (AECOPD). Most patients presenting with AECOPD in primary care are prescribed an antibiotic, which may not always be appropriate and may cause harm. Current antibiotic prescribing recommendations for general practitioners (GPs) are generally based on symptoms alone (Anthonisen criteria). However, these symptoms are subjective and are not enough to predict which patients can safely be managed without antibiotics. C-reactive protein (CRP) is a protein found in the blood that can be rapidly measured at the point of care and may predict benefit from antibiotic treatment in AECOPD. Point of care tests (POCTs) for acute infections are being promoted to reduce inappropriate prescribing, reduce antibiotic resistance and to improve patient outcomes, but the benefits of CRP POCT in conjunction with clinical examination have not yet been tested for AECOPD in primary care. The aim of this study is to find out whether the addition of a CRP POCT (with training on test use and advice on interpretation) to usual care for managing an AECOPD leads to a reduction in antibiotic consumption for AECOPD without negatively impacting on COPD health status, compared with usual care alone.

Who can participate?

Adults over the age of 40 with an acute exacerbation of COPD that has lasted between 24 hours to 21 days

What does the study involve?

Participants are randomly allocated to either clinical management based on usual care, or usual

care with the addition of a CRP POCT. The clinician records the number of days the participant reports having symptoms from the acute exacerbation, their medical history, and clinical examination results. A sputum sample (when participants are able to produce sputum) and throat swab samples (using charcoal swabs) are obtained from the participant. The clinicians assess and record the colour of the participant's sputum. Participants are asked to complete questionnaires. The CRP test results are recorded for those allocated to care with the addition of the CRP POCT. Antibiotic prescribing and other management decisions are recorded for all participants. The trial team aim to telephone all participants one week and two weeks later to collect information on their medication usage during that time and also to obtain their responses to questionnaires. Participants are invited to return to the surgery for a face-to-face consultation after four weeks. The following data are collected at the week 4 appointment: medication consumption, adverse effects, time off paid work, diagnosis of pneumonia since the first appointment, any further CRP tests since the first appointment, healthcare consultations. Sputum (where possible) and throat swab samples are obtained from the participant and the colour of the sputum is assessed. Participants are asked to complete questionnaires. More questionnaires are posted to participants for completion and return after 6 months.

What are the possible benefits and risks of participating?
Possible benefits include avoiding unnecessary antibiotics and therefore any adverse effects from taking them, using antibiotics appropriately when they are likely to be beneficial, closer monitoring and follow-up by the GP, and developing awareness around the prudent use of antibiotics for AECPOD and in general for the patients and GPs. Potential risks include the GP withholding antibiotic treatment from participants with a low CRP value. However, all participating sites are provided with information on current best practice. The GPs would be free to use antibiotics if they think this to be appropriate regardless of CRP values. Many cases of acute exacerbations are routinely treated without antibiotics at the moment, especially when the GP feels that the exacerbation is not likely to be caused by bacteria. The CRP test could help in making better decisions about antibiotic prescriptions.

Where is the study run from?
GP practices in Wales, Thames Valley, London, Eastern CRN and North West Coast CRN (UK)

When is the study starting and how long is it expected to run for?
November 2014 to July 2017

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

Who is the main contact?
Prof. Chris Butler
christopher.butler@phc.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Chris Butler

Contact details
Nuffield Department of Primary Care Health Sciences
University of Oxford
Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG
+44 (0)1865 289363
christopher.butler@phc.ox.ac.uk

Type(s)
Scientific

Contact name
Ms Janine Bates

ORCID ID
https://orcid.org/0000-0003-3610-2415

Contact details
South East Wales Trials Unit
Centre for Trials Research
Cardiff University
7th Floor
Neuadd Meirionnydd
Heath Park
Cardiff
United Kingdom
CF14 4XW
-
PACE@cardiff.ac.uk

Additional identifiers

Protocol serial number
SPON 1189-12; HTA 12/33/12

Study information

Scientific Title
Primary care use of a C-Reactive Protein (CRP) Point of Care Test (POCT) to help target antibiotic prescribing to patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) who are most likely to benefit: a two-arm individually randomised controlled trial

Acronym
PACE

Study objectives

Current hypothesis as of 21/02/2017:
Using a C-Reactive Protein point of care test in addition to usual care in managing acute exacerbations of Chronic Obstructive Pulmonary Disease will reduce antibiotic consumption without negatively affecting patient recovery as compared to usual care alone.

Previous hypothesis:
Using a C-Reactive Protein (CRP) point of care test (POCT) in addition to current best clinical practice in managing acute exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) will reduce antibiotic consumption without negatively affecting patient recovery as compared to current best clinical practice alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC 6, 15/09/2014, ref: 14/WA/1106

Study design
Two-arm individually randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute exacerbation of chronic obstructive pulmonary disease (AECOPD)

Interventions
Current interventions as of 21/02/2017:
PACE will assess the use of a CRP POCT to guide antibiotic treatment decisions for patients presenting in primary care with AECOPD. Patients randomised to the intervention arm will have a CRP POCT at every consultation for AECOPD that occurs in the four weeks following randomisation. Control patients will not have a CRP POCT (as part of this study) at any time during their participation.

Previous interventions:
PACE will assess use of a C-reactive protein (CRP) point-of-care test (POCT) to guide antibiotic treatment decisions for patients presenting in primary care with AECOPD. Participants will be allocated to a usual clinical care or an intervention arm. Patients randomised to the intervention arm will have a CRP test at every consultation for AECOPD that occurs in the four weeks following randomisation. Control patients will not have a CRP test (as part of this study) at any time during their participation.

The CRP POCT is developed by Alere. The test requires 1.5ìl of capillary blood (finger prick sample) and takes less than 4 minutes to provide a quantitative result.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Current primary outcome measures as of 21/02/2017:
The PACE study has co-primary outcomes:
1. Antibiotic consumption (any consumption of antibiotics for AECOPD vs. no consumption of antibiotics for AECOPD) within four weeks post-randomisation
2. Recovery in terms of COPD health status, assessed using the clinical COPD questionnaire (CCQ) total scores at two weeks post randomisation

Previous primary outcome measures:
This study is based on two co-primary outcomes:
1. Antibiotic consumption at any point during the four weeks post-randomisation, measured using telephone interviews at one-week and two-weeks and face-to-face interview at four-weeks
2. Patient-reported health-related quality of life (HRQoL) measured by the Chronic Respiratory Questionnaire Self-Administered Standardised (CRQ-SAS) via telephone interview at two-weeks

Key secondary outcome(s))
Current secondary outcome measures as of 21/02/2017:
1. Prevalence of potentially pathogenic bacteria (incl. S.pneumoniae, H.spp and Enterobacteriacae) and the proportion of bacteria that are resistant, cultured from sputum at 4 weeks post randomisation
2. Prevalence of commensal organisms and the proportion of bacteria that are resistant, cultured from throat swabs at 4 weeks post randomisation
3. COPD health status over time, measured using the CCQ total score measured at weeks 1, 2 and 4 post randomisation
4. CCQ symptoms domain at weeks 1, 2, and 4 post randomisation
5. CCQ function state domain at weeks 1, 2, and 4 post randomisation
6. CCQ mental state domain at weeks 1, 2, and 4 post randomisation
7. Total antibiotic consumption (number of days antibiotics consumed for AECOPD/any reason) during first 4 weeks post randomisation
8. Health utility, measured using the EuroQol-5D (EQ-5D) at weeks 1, 2 and 4 and at month 6 post randomisation
9. All cause antibiotic consumption during the first four weeks post randomisation
10. Antibiotic prescribing at the index consultation
11. Antibiotic prescribing during the first four weeks post randomisation
12. Use of other COPD treatments including oral steroids during the first four weeks post randomisation
13. Adverse effects potentially attributable to antibiotics prescribed for the exacerbation during the first four weeks post randomisation
14. Primary and secondary care consultations, including hospitalisations at week 4 and month 6
15. Costs (total NHS cost) and cost-effectiveness at month 6
16. Incidence of pneumonia, measured by patient and GP report at week 4 and month 6
17. Disease-specific health-related quality of life over time, measured using CRQ-SAS (dyspnoea, fatigue, emotion function, mastery and total scores) at month 6

Previous secondary outcome measures:
1. Prevalence of significant antibiotic resistant organisms (including Streptococcus spp., H. influenzae and parainfluenzae and Enterobacteriaceae) cultured from sputum or throat swab at 4 weeks

2. Disease-specific health-related quality of life over time measured using CRQ-SAS (measured at weeks 1, 2 and 4)
3. Health utility measured using the EuroQol-5D (EQ-5D) (measured at weeks 1, 2 and 4)
4. Antibiotic prescribing at the index consultation
5. Use of other COPD treatments including oral steroids (measured at weeks 1, 2 and 4)
6. Adverse effects potentially attributable to antibiotics prescribed for their exacerbation (nausea, vomiting, diarrhoea, thrush, and rash) (measured at weeks 1, 2 and 4)
7. Primary and secondary care consultations, including hospitalisations (measured at month 6)
8. Costs (total NHS cost) and cost-effectiveness (measured at month 6)
9. Incidence of pneumonia (measured by patient and GP report at week 4 and month 6)

Completion date
31/01/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/02/2017:
1. Has a current acute exacerbation [presenting with at least one of the following: Increased dyspnoea, increased sputum volume, increased sputum purulence] that has lasted for at least 24 hours and no longer than 21 days
2. Diagnosis of COPD in clinical record/on COPD Practice register
3. Age 40 years or more
4. Able to provide informed consent
5. Patient should be able to provide the primary outcome data at 2 and 4 weeks within the expected windows

Previous inclusion criteria:
1. Adults aged 40
2. Spirometry confirmed (at any time point prior to admission) COPD (post bronchodilator FEV1 /FVC < 0.7)
3. Patients with mild, moderate and severe disease: that is FEV1 of more than 30% of the predicted value as indicated by the age and the height of the person (GOLD stage 1-3)
4. Have a current AECOPD, defined as, an event in the natural course of the disease characterized by a change in the patient's baseline dyspnoea, cough and/or sputum that is beyond normal day-to-day variations, is acute in onset and may warrant a change in regular medication
5. The exacerbation has lasted for at least 24 hours but equal to or less than 21 days
6. Are able to attend the GP surgery
7. Are able to provide informed consent and complete study procedures.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex

All

Total final enrolment
653

Key exclusion criteria
Current exclusion criteria as of 21/02/2017:
1. The responsible GP feels urgent referral to hospital is necessary
2. Severe illness (e.g. suspected pneumonia, tachypnoea >30 breaths per minute, respiratory failure)
3. Concurrent infection at another site (e.g. UTI, Cellulitis) that is likely to produce a systemic response
4. Past history of respiratory failure or mechanical ventilation
5. Currently on antibiotics or has had antibiotics for this acute exacerbation of COPD
6. Active inflammatory condition (e.g. Flare up of rheumatoid arthritis, gout or polymyalgia rheumatica)
7. Has cystic fibrosis, a current tracheostomy or bronchiectasis
8. Immunocompromised (e.g. AIDS, taking systemic immunosuppressive therapy or receiving anti-cancer radiotherapy or chemotherapy)
9. Currently pregnant
10. Previously been recruited into the PACE study

Previous exclusion criteria:
1. Very severe COPD (GOLD stage 4; FEV1 < 30% predicted)
2. Coexisting infection (i.e. urinary tract infection, cellulitis)
3. Suspected pneumonia or requiring immediate hospital admission
4. History of requiring mechanical ventilation for an AECOPD
5. Active chronic inflammatory condition (i.e. rheumatoid arthritis)
6. Currently already taking high dose oral steroids (equivalent to 60mg per day or more of prednisolone)
7. Has taken oral antibiotics in previous four weeks
8. Life limiting malignancy
9. Cystic fibrosis
10. Current tracheotomy
11. Bronchiectasis of any aetiology other than COPD
12. Previously been recruited into the PACE study

Date of first enrolment
22/01/2015

Date of final enrolment
17/02/2017

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
South East Wales Trials Unit
Centre for Trials Research
College of Biomedical and Life Sciences
Cardiff University
Cardiff
United Kingdom
CF14 4YS

Study participating centre
The Nuffield Department of Primary Care Health Sciences
University of Oxford
Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG

Study participating centre
Department of Primary Care & Public Health Sciences
King's College London
London
United Kingdom
SE1 3QD

Sponsor information

Organisation
Cardiff University (UK)

ROR
https://ror.org/03kk7td41

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
The datasets generated during and/or analysed during the current study are/will be available upon request from opendata@cardiff.ac.uk – this would be at the end of the study. The aim is to make the research data available wherever possible, subject to regulatory approvals, any terms and conditions from external providers, patient confidentiality and all laws concerning the protection of personal information. Data is generally freely available, but recipients are expected to acknowledge the original creators in any public use of the data or in publishing research results based wholly or in part upon the data – anyone requesting access to data will be asked to agree to the terms of the Creative Commons Attribution 4.0 license. The trialists may ask the requestor to cover reasonable cost for preparing and providing the data (for example physical storage and postage, where dataset size makes it impractical to provide data by electronic means).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	11/07/2019	26/07/2019	Yes	No
Results article	results	01/03/2020	24/03/2020	Yes	No
Results article	Cost effectiveness at 6 months	27/11/2024	03/12/2024	Yes	No
Protocol article	protocol	29/09/2017		Yes	No
HRA research summary			28/06/2023	No	No
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