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The effectiveness of antibiotics compared to no antibiotics for exacerbations of chronic obstructive pulmonary disease: a feasibility study

Submission date
12/03/2010

Recruitment status
No longer recruiting

Registration date
15/03/2010

Overall study status
Completed

Last Edited
25/05/2016

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
This study will evaluate whether antibiotic treatment is beneficial in patients with chronic lung disease who experience a sudden increase in shortness of breath and coughing. The study will be run within and use data from the General Practice Research Database, which for analysis purposes contains anonymised medical records of over 3 million "active" patients. This database is being widely used for observational research, particularly to evaluate the adverse effects of medicines. This database collects information on the healthcare provided to these patients by the general practitioners and on any hospital admissions.

Who can participate?
Patients aged 40 or older with chronic obstructive pulmonary disease

What does the study involve?
Eligible patients are asked by their GPs to consent to participation into the study. After the patient's consent, the record is flagged and they are randomly allocated to receive either antibiotic treatment or no treatment. Patients are then followed and routine medical care is provided to them as needed. The information collected for the patients mostly consists of information that is routinely collected by GPs and others in primary care. This includes information on the patient returning to the GP for symptoms related to lung disease. It also includes information about hospital admissions or prescribing of other medicines for this condition.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Medicines & Healthcare Products Regulatory Agency (UK)

When is the study starting and how long is it expected to run for?
July 2010 to July 2012

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
HTA 07/50/05; 10_022

Study information

Scientific Title
Antibiotics for Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD): a pilot randomised trial within the General Practice Research Database (GPRD)

Acronym
AECOPD

Study objectives
Randomised clinical trials have made major contributions to medical research. But the costs of conducting these studies can often be prohibitive. A considerable amount of the data needed in prospective studies is increasingly collected as part of routine health care. A major opportunity in extending research opportunities could be for trials to use information that is routinely collected. A randomised clinical trial could be conducted by prospectively randomising participants to treatment with subsequent data collection and follow up conducted by using the routinely collected data (also known as 'randomised clinical trial within the database' [RCTdb]).

This type of study evaluates the drug effectiveness (i.e., the outcomes within routine health care system) rather than drug efficacy (i.e., the outcomes in ideal circumstances).

This will be a feasibility trial of RCTdb. General Practitioners (GPs) play a key role in the UK health care system, as they are responsible for primary health care and specialist referrals. Hospitals are required to inform GPs of any significant medical events that occur. Long-term care of chronic conditions is typically managed by GPs. As a consequence, medical records as managed by the GPs contain longitudinal information on all significant medical events and prescribing. They are essentially the life-long record for each patient and include the key secondary care information as well laboratory, other investigations and details of all medications prescribed within general practice. Data from practices in England can now be linked anonymously at the person level to various other NHS datasets, including the death certificates, the national registry in England of hospital admission, prospective disease registries (such as the cancer registries or the Central Cardiac Audit Database, that records, among others clinical details on subjects admitted to hospitals in England for myocardial infarction). These records contain unique information for research.

Chronic obstructive pulmonary disease (COPD) is a progressive condition characterised by an obstructive pattern of expiratory airflow limitation which can not be fully reversed. Patients with COPD frequently suffer from acute exacerbations of the disease, characterised by an increase in symptoms of dyspnoea, sputum volume or purulence. COPD exacerbations are often bacterial in origin and antibiotic therapy is appropriate. However, COPD exacerbations may also be due to viral infections of the upper respiratory tract or may be non-infective. The role of antibiotics in treating mild or moderate acute COPD exacerbations without purulent sputum is not clear.

Most randomised clinical trials (RCTs) evaluating antibiotics for COPD are restricted to patients hospitalised for acute exacerbations. Of the 11 studies included in a recent Cochrane review only two included patients from a GP setting, despite much healthcare for COPD patients being administered in this environment. Also, few of the studies provided details on the resource utilisation associated with exacerbations or the effect of prescribing antibiotics on this utilisation. Given the very high costs associated with conducting large paper-based RCTs the largest study to date included just 270 patients. There is a clear need for a method of conducting large cost-effective RCTs in general clinical practice.

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/075005
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0005/51872/PRO-07-50-05.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multicentre pragmatic randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Potentially eligible trial subjects will be identified by the Principal Investigator within the anonymous GPRD records. These will be patients with a spirometry confirmed diagnosis of COPD using the definitions of the Quality and Outcomes Framework (QOF). QOF was implemented in 2004 and established reimbursement for reporting indices related to selected diseases, including COPD. Trial recruitment procedures will be initiated for potentially eligible trial subjects (using a flagging system in the GP software) if the patient visits the GP Investigator. If the patient suffers from an acute COPD exacerbation with an increase of non-purulent sputum volume, the GP Investigator will then review and confirm the eligibility criteria and record this in the electronic case report form in a web-based secure clinical trial management system. For patients that accept to participate in the study, the system will allow printing a consent form for the patient to sign. The information about this study will be provided at the point of consultation by the GP Investigator. It is stated on the information sheet that a subject can withdraw at any stage or not redeem the antibiotic.

Consenting patients can be provided with an antibiotic prescription at the same visit as the recruitment. But consenting patients will be informed that they can 'opt-out' of the study by not redeeming the prescription for the study drug and that they can return for a consultation.

After 4 weeks after the baseline visit, trial participants will be invited to visit the general practice. They will be requested to return with the completed patient diary. Trial subjects will be followed for a period of 3 months for study outcomes:
1. Hospital admission for COPD exacerbation
2. All-cause mortality
3. Prescribing of antibiotics
4. Suspected adverse drug reactions to the study drug
5. NHS costs for secondary outcomes

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Measuring the feasibility of conducting RCTdb; after randomisation to treatment or no treatment, patients will be followed using information collected in GPRD. The feasibility evaluation will include the recruitment rate and an assessment of the technical challenges in conducting RCTdb. No formal threshold for success will be applied but results will be published.

Key secondary outcome(s))
Over the first four weeks:
1. Participants will be requested to complete a daily diary (i.e. the Exacerbations of Chronic Pulmonary Disease Tool: a validated assessment tool to quantify the frequency, severity and duration of COPD exacerbations)

2. Repeat GP visit for symptoms related to the same COPD exacerbation in the 4-week period
3. Referrals to community respiratory team in the 4-week period
4. Hospital admission for COPD exacerbation in the 4-week period
5. Prescribing of oral corticosteroids in the 4-week period

Over 3 months:
6. Hospital admission for COPD exacerbation
7. All-cause mortality
8. Prescribing of antibiotics
9. Suspected adverse drug reactions to the study drug
10. NHS costs for secondary outcomes

Given the small number of participants in this study, these secondary outcomes will serve as pilot data for power calculations for larger studies in the future. The study will not be powered statistically to detect a difference in secondary outcomes.

Completion date
12/07/2012

Eligibility

Key inclusion criteria
1. Aged 40 years or older, either sex
2. Diagnosed at a GP visit as suffering from acute exacerbation of COPD:
2.1. Medical history of COPD
2.2. Increase in dyspnoea and increase of (non-purulent) sputum volume
3. Able and willing to provide informed consent to study participation
4. Fully registered with the general practice for at least 6 months (i.e. subjects who are newly registered with the practice will not be eligible)
5. Subjects who had not been prescribed an antibiotic in the previous 3 months
6. Subjects who in the opinion of the GP Investigator could be prescribed an antibiotic

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Purulent sputum (as determined by GP)
2. COPD exacerbation in the last 28 days
3. Immediate referral to specialist care for treatment of COPD exacerbation
4. Prescribed an antibiotic in the previous 3 months
5. Contra-indication to antibiotics. Further details can be found in the British National Formulary (section 5).

Date of first enrolment
12/07/2010

Date of final enrolment
12/07/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
GPRD
London
United Kingdom
SW8 5NQ

Sponsor information

Organisation
London School of Hygiene and Tropical Medicine (LSHTM) (UK)

ROR
https://ror.org/00a0jsq62

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2014		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes