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# Angiotensin converting enzyme (ACE) inhibition and mechanisms of skeletal muscle weakness in chronic obstructive pulmonary disease (COPD)

**Submission date**
26/06/2008

**Recruitment status**
No longer recruiting

**Registration date**
31/10/2008

**Overall study status**
Completed

**Last Edited**
13/02/2020

**Condition category**
Respiratory

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

**Plain English summary of protocol**
Not provided at time of registration

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**
NCT01014338

**Secondary identifying numbers**

MRC ref: G0701628; IC-DHTAX_P15099

# Study information

### Scientific Title
Angiotensin converting enzyme (ACE) inhibition and mechanisms of skeletal muscle weakness in chronic obstructive pulmonary disease (COPD): a double-blind, randomised, placebo-controlled, parallel trial

### Study objectives
That angiotensin converting enzyme (ACE) inhibition will improve muscle function in patients with chronic obstructive pulmonary disease (COPD) who have leg weakness. Muscle function will be assessed in terms of strength and endurance. Changes in muscle function (strength and endurance) will be related to changes in the molecular pathways which are thought to be involved in muscle wasting in COPD.

As of 17/02/2009 this record was updated to include a change to the ACE-I drug used. more details of this can be found in the interventions section. At this time, the anticipated trial dates were also updated; the initial trial dates at the time of registration were:
Initial anticipated start date: 01/10/2008
initial anticipated end date: 30/09/2011

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
The study has been approved by the Joint UCL/UCLH Committees on the Ethics of Human Research Committee Alpha on the 2nd October 2008 (ref: 08/H0715/90)

### Study design
A double-blind, randomised, placebo-controlled, parallel trial

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Hospital

### Study type(s)
Treatment

### Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

### Interventions
Amended as of 17/02/2009:
10 or 20 mg of fosinopril per day for three months, versus placebo on same administrative routine.

Initial information at time of registration:
Imidapril tablets (ACE-I) up to 20 mg per day for three months, versus placebo on same administrative routine.

### Intervention Type
Drug

### Phase
Not Specified

### Drug/device/biological/vaccine name(s)
Angiotensin converting enzyme inhibitor (ACE-I) (Imidapril)

### Primary outcome measure
Primary analysis will focus on the activity of the insulin-like growth factor-1 (IGF-1) Akt pathways controlling muscle catabolism and anabolism assessed in muscle biopsies. Measurements will include phosphorylated and non-phosphorylated Akt and mammalian target of rapamycin (mTOR) as well as myogenic differentiation factor (MyoD), muscle-specific RING-finger protein (MuRF) and atrogin-1 messenger ribonucleic acid (mRNA) and protein levels. Changes in these pathways will be related to changes in muscle phenotype. These measurements will be made in muscle biopsies taken at baseline and after three months of treatment.

### Secondary outcome measures
The following will be assessed in muscle biopsies taken at baseline and after three months of treatment:
1. Effect of ACE-I on quadriceps maximum voluntary contraction force
2. Effect of ACE-I on quadriceps endurance: T80 Time for force output in response to stimulation
3. Effect of ACE-I on quadriceps bulk (cross-sectional area)
4. Effect of ACE-I on systemic inflammation and serum IGF-1

At the initial screening assessment patients biopsies will have been obtained from patients who are not weak and therefore ineligible for this trial. Data from these patients will be compared cross-sectionally with the weaker patients to compare activity of the molecular pathways mentioned above and related to muscle phenotype.

### Overall study start date
01/06/2009

### Completion date
01/05/2012

## Eligibility

### Key inclusion criteria

Adult patients (greater than 18 years, either sex) with COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Only patients with quadriceps weakness will be enrolled into this randomised controlled trial (RCT).

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
80

### Key exclusion criteria
1. Clinically unstable patients (within one month of exacerbation)
2. Those with a permanent pacemaker (which is a contraindication to magnetic stimulation), or significant co-morbidity
3. Patients with an accepted indication for ACE inhibition (left ventricular dysfunction, diabetes) or a contraindication such as renovascular disease
4. Creatinine clearance (estimated) less than 50 ml/min
5. Hypotension
6. Use of anticoagulants (contraindication to biopsy) or angiotensin converting enzyme inhibitor (ACE-I) or angiotensin II (ATII) receptor antagonists
7. Allergy to ACE-I
8. Pregnancy
9. Patients who have participated in a pulmonary rehabilitation programme within the past three months

### Date of first enrolment
01/06/2009

### Date of final enrolment
01/05/2012

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre

**Royal Brompton Hospital**
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# Sponsor information

**Organisation**
Imperial College London (UK)

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**Sponsor type**
University/education

**Website**
http://www3.imperial.ac.uk/

**ROR**
https://ror.org/041kmwe10

# Funder(s)

**Funder type**
Research council

**Funder Name**
Medical Research Council (MRC) (UK) (ref: G0701628)

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type**
Government organisation

### Funding Body Subtype
National government

### Location
United Kingdom

# Results and Publications

### Publication and dissemination plan
Not provided at time of registration

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not provided at time of registration

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | results | 01/10/2014 | | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |