

# ON-EPIC Oral nitrate supplementation to enhance pulmonary rehabilitation in chronic obstructive pulmonary disease

<b>Submission date</b> 22/09/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 29/10/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 19/11/2020	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Chronic obstructive pulmonary disease (COPD) is the name of a group of lung diseases (including emphysema and chronic bronchitis) that cause breathing difficulties due mostly to narrowing of the airways. It is most often caused by smoking and results in breathlessness, persistent coughing and recurrent chest infections. Even with excellent treatment, patients often find themselves significantly disabled by the disease. Pulmonary rehabilitation is a proven therapy for COPD where patients are placed on a 8 week programme which includes supervised exercise sessions and learning about their condition. However, places are limited and so its important to get as much benefit from them as possible. A number of studies have shown that increasing the amount of dietary nitrate in the diet makes exercise easier and less tiring. This is because dietary nitrates are converted into another compound called nitric oxide which widens blood vessels and reduces the amount of oxygen needed the muscles. Beetroot juice is a good source of dietary nitrate. We want to find out whether increasing the amount of nitrate in the diet (in the form of beetroot juice) can help to improve how patients respond to the pulmonary rehabilitation programme.

### Who can participate?

Patients with COPD that may benefit from the pulmonary rehabilitation programme.

### What does the study involve?

Participants are randomly allocated into one of two groups. Those in group 1 are given beetroot juice to drink. Those in group 2 are given a placebo (without nitrate). We then compare improvements in the amount of exercise they can do after they have all attended a pulmonary rehabilitation programme. This is tested with a shuttle walking test which measures how far and how fast each participants can walk without having to stop and rest. The participants are also asked to fill in questionnaires designed to assess their state of health. Flow mediated dilatation measurements, which see how responsive their blood vessels are also taken from some participants.

What are the possible benefits and risks of participating?

No risks are anticipated. Possible benefits include general improvement to health and being able to exercise for longer periods.

Where is the study run from?

Royal Brompton and Harefield NHS Foundation Trust (UK)

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

January 2015 to April 2018

Who is funding the study?

The JP Moulton Medical Foundation (UK)

Who is the main contact?

Dr Nicholas Hopkinson

n.hopkinson@ic.ac.uk

## Contact information

**Type(s)**

Scientific

**Contact name**

Dr Nicholas Hopkinson

**Contact details**

Royal Brompton Hospital

Fulham Rd

London

United Kingdom

SW3 6NP

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

2

## Study information

**Scientific Title**

ON-EPIC Oral nitrate supplementation to enhance pulmonary rehabilitation in chronic obstructive pulmonary disease: a multi-centre, double blind, placebo-controlled, cross-over study

**Acronym**

ON-EPIC

### **Study objectives**

The purpose of this study is to investigate the effects of administration of beetroot (BR) juice versus placebo beverage ingestion on exercise tolerance, health status, blood pressure, plasma NO<sub>2</sub><sup>-</sup> levels, after attendance at a pulmonary rehabilitation.

The following hypotheses are to be tested:

1. BR would increase incremental shuttle walk test distance after completion of PR
2. BR would increase health related quality of life scores after completion of PR
3. BR would decrease fat mass after completion to PR
4. BR would increase plasma NO<sub>2</sub><sup>-</sup> levels (a biomarker of NO production and availability)

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

NRES Committee London - London Bridge, 1/10/2014, Ref: 14/LO/1474

### **Study design**

Multi-centre double-blind placebo-controlled cross-over study

### **Primary study design**

Interventional

### **Secondary study design**

Randomised cross over trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

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

### **Health condition(s) or problem(s) studied**

Chronic obstructive pulmonary disease (COPD)

### **Interventions**

Beetroot juice drink or matched nitrate-depleted placebo.

### **Intervention Type**

Other

### **Phase**

Not Applicable

### **Primary outcome measure**

Incremental shuttle walking test (ISWT) distance

### **Secondary outcome measures**

All outcomes measured at 8 weeks:

1. Health status measured by the COPD assessment test score (CAT) and the Hospital Anxiety and Depression scale (HADS)
2. Fat free mass determined by bioelectrical impedance analysis
3. Flow mediated dilatation (FMD)

Removed 16/04/2018:

4. Blood plasma NO<sub>2</sub> levels (a marker of NO production and availability) as an exploratory variable

### **Overall study start date**

15/01/2015

### **Completion date**

01/04/2018

## **Eligibility**

### **Key inclusion criteria**

Patients will need to have a clinical and spirometric diagnosis of COPD, GOLD stage II-IV and with an MRC score of 3-5 or to be functionally limited

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Both

### **Target number of participants**

140

### **Total final enrolment**

165

### **Key exclusion criteria**

1. Clinically unstable patients (within one month of exacerbation)
2. Within one month of completing pulmonary rehabilitation
3. Significant comorbidity limiting exercise tolerance
4. Significant renal impairment (estimated glomerular filtration rate (eGFR) <50 ml.min<sup>-1</sup>)
5. Hypotension (systolic blood pressure <100 mmHg)
6. Pregnancy
7. Use of nitrate based medication

8. Other reason for benefit from nitrate supplementation (ischaemic heart disease, peripheral arterial disease)

9. Use of long-term oxygen therapy

**Date of first enrolment**

26/01/2015

**Date of final enrolment**

01/11/2017

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Royal Brompton Hospital**

London

United Kingdom

SW3 6NP

## **Sponsor information**

**Organisation**

Imperial College, London (UK)

**Sponsor details**

c/o Christine Buicke

AHSC Joint Research Compliance Office

510, 5th Floor Lab Block

Imperial College

London

England

United Kingdom

W6 8RF

-

c.buicke@imperial.ac.uk

**Sponsor type**

University/education

**ROR**

<https://ror.org/041kmwe10>

# Funder(s)

## Funder type

Research organisation

## Funder Name

JP Moulton Medical Foundation (UK)

# Results and Publications

## Publication and dissemination plan

Publication is planned in a high-impact peer reviewed journal.

## Intention to publish date

01/06/2020

## Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

## IPD sharing plan summary

Other

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/07/2020	19/11/2020	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No