

# Genomics to combat resistance against antibiotics for community-acquired lower respiratory tract infection (LRTI) in Europe (GRACE) work package 10: Antibiotic Trial One

<b>Submission date</b> 02/12/2008	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/01/2009	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 06/11/2015	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

This study is part of a programme of research into cough/chest infections across 12 European countries. Most people with chest infections probably don't benefit from antibiotics and inappropriate antibiotic use drives antibiotic resistance, a major global health problem. Some groups of people however might really benefit from antibiotics. The study aims at understanding which subgroups of individuals with chest infections benefit from antibiotics, but also to study antibiotic resistance after antibiotic treatment.

### Who can participate?

Throughout Europe 3000 adult patients presenting to primary care with acute cough or other symptoms that suggest a chest infection will take part in this study.

### What does the study involve?

If the participating doctors think there is no definite need for antibiotics, participants will be asked to take a 7-day course of tablets to be taken three times a day. The tablets will be either amoxicillin, a very commonly used and safe penicillin-based antibiotic, or a placebo (a tablet without any medication in it). They will not be able to tell whether they will have the real antibiotic or the placebo. Random numbers are used to decide whether participants get antibiotic or placebo to make sure that they have an equal chance of getting either. This is the best way for us to show scientifically whether antibiotics really make a difference. If it is necessary to know whether participants are using an antibiotic or not, the participating doctors will be able to get that information at any time and change the participant's medication. The participating doctors will also like to take one throat swab at day 8 (extra visit) and at the second study visit (day 28-35). The swab at day 8 will not be taken in all participants. If participants decide they do not want to have a swab taken at day 8 they can still take part in the treatment part of the study.

What are the possible benefits and risks of participating?

The main advantage is that the participating doctors will be well informed about the participants' illness and will monitor them closely. In the future doctors will be able to provide better management for patients with coughs and chest infections, but this will not benefit the participants during this illness. The main disadvantages are the extra time and discomfort related to taking the additional swabs. The patients who will receive amoxicillin can experience the usual side-effects of penicillin: it can cause mild nausea or diarrhoea, and sometimes it can cause a transient skin rash.

Where is the study run from?

University of Southampton (UK).

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

October 2007 to April 2010.

Who is funding the study?

EC Sixth Framework Programme.

Who is the main contact?

Prof Paul Little

#### **Study website**

<http://www.grace-lrti.org>

## **Contact information**

#### **Type(s)**

Scientific

#### **Contact name**

Prof Paul Little

#### **ORCID ID**

<http://orcid.org/0000-0003-3664-1873>

#### **Contact details**

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SO16 5ST

#### **Type(s)**

Scientific

#### **Contact name**

Dr Herman Goossens

#### **Contact details**

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2610

## Additional identifiers

### EudraCT/CTIS number

2007-001586-15

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

GRACE WP10 Protocol v4.1 18/09/2007; GRACE WP10 Protocol v4.2 21/4/2009 (to extend the study with additional networks and a third inclusion period and, only in five networks in the third inclusion period, with an additional objective with associated samples)

## Study information

### Scientific Title

Genomics to combat Resistance against Antibiotics for Community-acquired lower respiratory tract infection (LRTI) in Europe (GRACE) work package 10: Antibiotic Trial One - a randomised placebo-controlled double-blind trial

### Acronym

GRACE AT ONE

### Study objectives

This trial aims at understanding which subgroups of individuals with lower respiratory tract infections (LRTI) benefit from antibiotics. A randomised placebo-controlled double-blind trial will be carried out with patients as unit of randomisation to study the clinical effectiveness of antibiotics in community-acquired LRTI.

More details can be found at: <http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=4175>

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

GRACE WP10 Protocol v4.1: Southampton and South West Hampshire REC (B), 31/08/2007, ref: 07/H0504/104

GRACE WP10 Protocol v4.2: amendment approved 21/04/2009

The study protocols were approved by ethics committees in all participating countries. The competent authority in each country also gave their approval.

**Study design**

Randomised placebo-controlled double-blind trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

GP practice

**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**

Lower respiratory tract infection (LRTI)

**Interventions**

1. Amoxicillin capsule, gastroenteral use, 3 g a day for 7 days
2. Placebo

**Intervention Type**

Drug

**Phase**

Phase III

**Drug/device/biological/vaccine name(s)**

Amoxicillin

**Primary outcome measure**

1. Deterioration of illness: return to doctor with worsening signs, or admission to hospital within 4 weeks of first consultation, measured at one year
2. Symptom severity and duration, duration of symptoms rated moderately bad until symptoms clear, measured by symptom diary (with construct validity), measured at one year

**Secondary outcome measures**

1. Resource use data, assessed by a review of clinical notes measured at two years
2. Quality of life outcomes for use of economic evaluation (EQ5D), measured at two years

Added 25/11/2014:

3. Antibacterial resistance in oropharyngeal streptococci measured before, immediately after and four weeks after the interventions in five networks in the third inclusion period

**Overall study start date**

17/03/2006

**Completion date**

01/04/2010

## Eligibility

**Key inclusion criteria**

1. Aged 18 and over, either sex
2. Acute or worsened cough is the main presentation suggesting LRTI, less than 28 days duration
3. Not been included earlier in the current GRACE trial
4. Able to fill out study materials
5. Immunocompetent
6. Not been on antibiotic treatment in previous month
7. First consultation for this illness episode

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

3000

**Key exclusion criteria**

1. Allergic to penicillin
2. History/physical examination suggestive of community acquired pneumonia (CAP)
3. Pregnant

**Date of first enrolment**

15/11/2007

**Date of final enrolment**

14/04/2010

## Locations

**Countries of recruitment**

Belgium

England

France

Germany

Italy

Netherlands

Poland

Slovakia

Slovenia

Spain

Sweden

United Kingdom

**Study participating centre**  
**University of Southampton**  
Southampton  
United Kingdom  
SO16 5ST

## **Sponsor information**

### **Organisation**

University of Southampton (UK)

### **Sponsor details**

Research Governance Office  
George Thomas Building 37  
Room 4001  
Highfield  
Southampton  
England  
United Kingdom  
SO17 1BJ

### **Sponsor type**

University/education

### **Website**

<http://www.soton.ac.uk/>

**ROR**

## Funder(s)

### Funder type

Government

### Funder Name

Sixth Framework Programme

### Alternative Name(s)

EC Sixth Framework Programme, European Commission Sixth Framework Programme, EU Sixth Framework Programme, European Union Sixth Framework Programme, FP6

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

## Results and Publications

### Publication and dissemination plan

We plan to publish on the overall effect of amoxicillin for acute lower-respiratory-tract infection in primary care when pneumonia is not suspected and on a subgroup analysis of potential high-risk groups. Next we plan to publish on the cost-effectiveness of treatment with amoxicillin for acute lower-respiratory-tract infection in primary care and on the selection and persistence of antibiotic resistance in oral streptococci after such treatment.

Participant level data will be stored in a repository, the GRACE Database and Biobank, which is financially supported through the European Science Foundation (ESF), in the framework of the Research Networking Programme TRACE (Translational Research on Antimicrobial resistance and Community-acquired infections in Europe; [www.esf.org/trace](http://www.esf.org/trace)) and to consult via its chair Herman Goossens.

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Stored in repository

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/02/2013		Yes	No
<a href="#">Results article</a>	results	01/02/2014		Yes	No
<a href="#">Results article</a>	results	06/03/2015		Yes	No
<a href="#">Results article</a>	results	05/11/2015		Yes	No