

# Is it better to treat pneumonia by customising antibiotic treatment based on the PIBCAP test compared to the current standard NHS treatment?

<b>Submission date</b> 08/04/2019	<b>Recruitment status</b> Stopped	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 28/05/2019	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 01/12/2021	<b>Condition category</b> Respiratory	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

There is an international drive to simplify antibiotic treatments to stop side effects from antibiotics and to stop the development of superbugs. Pneumonia is an infection of the lung affecting 5 to 11 people out of 1,000 in the population. About 9% of patients admitted to hospital with pneumonia will die. Prompt and appropriate antibiotic treatment is needed to cure the pneumonia. International guidelines suggest using a combination antibiotic treatment for 7 to 10 days for patients admitted with pneumonia. However, it is not completely known what antibiotics to prescribe or for how long antibiotic treatment is needed. By the time patients are admitted to hospital with pneumonia many of them will already have had antibiotics from their GPs. This can limit the results from standard pneumonia investigations. Tests currently used in the NHS can identify the cause of pneumonia in only 39% of patients. In addition, traditional methods to investigate pneumonia in the NHS take too long to give an answer. In many cases clinicians do not have enough information to confidently shorten or reduce antibiotic treatments. The researchers have developed a molecular test called a PIB CAP bundle that identifies the cause of pneumonia in 87% of patients. The test still works even if the patient has already started antibiotic treatment. The test is very quick and can have a result within a few hours. The main aim of this study is to determine if the PIB CAP test can reduce the amount of antibiotics prescribed without any undesirable clinical side effects.

### Who can participate?

Patients aged 16 and over who have been admitted to hospital with pneumonia

### What does the study involve?

Participants are randomly allocated to one of two groups. Half the participants have the usual NHS tests and receive the normal treatment for pneumonia. The other half of the participants have the new molecular test and the results customise their antibiotic treatment. The researchers assess how much antibiotic treatment each participant had, including any additional antibiotics that might have been needed after initial treatment. After 30 days each participant

has medical examinations and tests to see if it is safe to treat pneumonia with less antibiotics. It is also calculated if personalised antibiotic therapy is cost-effective for the NHS compared to the current treatment.

What are the possible benefits and risks of participating?

Participants may benefit from the additional tests and investigations that they will undergo as part of the study. However, as participants will be already receiving optimal NHS care there may be no direct benefit from participating in this study. It is not thought that there are any risks of participating.

Where is the study run from?

Five major centres in the UK (Edinburgh, Newcastle, Nottingham, Birmingham and London)

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

December 2017 to March 2021 (updated 12/04/2021, previously: March 2022)

Who is funding the study?

National Institute for Health Research (NIHR) (UK)

Who is the main contact?

PIBCAP Trials Office

pibcap@ed.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Miss Moira Ross

### Contact details

Trial Manager

Edinburgh Clinical Trials Unit

Usher Institute University of Edinburgh

Level 2, Nine Edinburgh BioQuarter

9 Little France Road

Edinburgh

United Kingdom

EH16 4UX

+44 (0)131 651 9910

pibcap@ed.ac.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Protocol serial number

41947

# Study information

## Scientific Title

Pneumonia investigation bundle to guide therapy for hospitalised community acquired pneumonia (PIBCAP study)

## Acronym

PIBCAP

## Study objectives

The primary objective is to explore whether participants admitted with community-acquired pneumonia can safely receive personalised antibiotic therapy within 36 hours of hospital admission. The researchers will also calculate if personalised antibiotic therapy is cost-effective for the NHS compared to the current treatment and they will also assess several secondary clinical endpoints.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Approved 17/10/2018, Scotland A REC (Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG; Tel: +44 (0)131 465-5680; manx.neill@nhslothian.scot.nhs.uk), ref: 18/SS/0125

## Study design

Randomised; Interventional; Design type: Treatment, Other

## Primary study design

Interventional

## Study type(s)

Treatment

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

Community-acquired pneumonia

## Interventions

This study is a pragmatic, multicentre, open randomised controlled trial. We will recruit from 5 UK hospitals. Participants will be identified by the clinical care team or research nurse by assessing those admitted to hospital with community-acquired pneumonia.

Eligible participants will randomised at baseline to either control treatment or the PIBCAP intervention:

1. The control arm will have investigations and treatment per NICE Pneumonia guideline.
2. The participants randomised to the PIBCAP arm will have PIBCAP investigations performed on their admission throat swab, spontaneous sputum (if available) and urine (if available). Initially this group will have standard antibiotic treatment as per NICE Pneumonia guideline, but then following PIB CAP results treatment will be personalised within 36 hours of hospital admission.

All participants will be asked to complete patient questionnaires and have clinical assessments recorded at baseline, 7 days and 30 days after enrollment. The day 7 visit is a safety assessment and the day 30 visit is to assess recovery. Interventions will be delivered by the clinical care team supported by the research nurse.

The primary outcome measure is the Desirability of Outcome Ranking (DOOR) to assess the efficacy and safety of PIB CAP therapy based on assessing (A) day 30 clinical response and (B) day 30 total antibiotics Defined Daily Dose (DDD) to ensure by narrowing antibiotics this does not lead to subsequent additional antibiotic use. This study will assess the utility of a pneumonia investigation bundle using fast multiplex real-time Polymerase Chain Reaction assays for 26 respiratory bacteria and viruses along with urine for Legionella Antigen test (using BinaxNOW®) to personalise antibiotic treatment within 36 hours of hospital admission. Twelve months after enrollment the researchers will use central NHS and GP records to electronically assess health care utilisation (i.e. record linkage for longitudinal follow up). Both cost-utility (CUA) and cost-effectiveness analysis (CEA) per reduction in antibiotic exposure will be assessed at 30 days and 1 year follow up.

## **Intervention Type**

Other

## **Primary outcome(s)**

Clinical outcome measured with Desirability of Outcome Ranking (DOOR) and then further ranked using the Response Adjusted for Duration of Antibiotic Risk, assessed at day 30

## **Key secondary outcome(s)**

1. CAP resolution (Y/N), measured by improvement of symptoms and clinical signs related to CAP, CRP level < 20 mg/L, and not on antibiotics related to CAP, assessed at day 7 and day 30
2. Major adverse events (Y/N) and number, measured by clinician reporting an event in medical records, assessed at day 7 and day 30
3. Readmissions to hospital within 30 days due to CAP, measured by admission recorded in patient records, assessed at day 30
4. Death (at 30 days and time to death), measured by death recorded in patient records, assessed at day 30
5. Narrowing spectrum of antibiotics, measured by clinician confirming that antibiotic prescriptions were altered according to PIBCAP results, assessed at day 7 and day 30
6. Macrolide DDD, measured by calculating the daily dose of macrolide antibiotics prescribed, assessed at day 30
7. Alteration or addition of antibiotic therapy, measured by antibiotic prescriptions in medical records, assessed at day 7 and day 30
8. Length of hospital stay, measured by admission and discharge dates recorded in patient records, assessed at day 7 and day 30
9. Antibiotic side effects, measured by clinician reporting an event in medical records, assessed at day 7 and day 30
10. Antibiotic costs measured within trial analysis and longer term economic modelling, assessed at day 30
11. Participant symptoms, measured by clinician reporting an event in medical records, assessed at day 7 and day 30
12. Antibiotic resistance in bacteria isolated, measured within trial analysis, assessed at day 30
13. The optimum specimen(s) for assessment of CAP for bacteria, atypical bacteria and viruses, measured within trial analysis, assessed at day 30
14. Cost per QALY at 30 days, measured within trial analysis and longer term economic

modelling, assessed at day 30

15. Cost per DDD of antibiotics at 30 days, measured within trial analysis and longer term economic modelling, assessed at day 30

Additional secondary outcome measures in the PIBCAP group:

1. Time to PIB, measured within trial analysis from times recorded in CRF, assessed at baseline
2. Whether clinicians personalise antibiotics based within 36 hours of hospital admission using the PIB CAP bundle CAP results, measured by within trial analysis and by clinician confirming a change in prescribing, assessed at day 7 and day 30
3. Proportion of PIB CAP that produces a result, measured within trial analysis from lab results recorded in patient medical record, assessed at baseline

### **Completion date**

31/03/2021

### **Reason abandoned (if study stopped)**

Participant recruitment issue

## **Eligibility**

### **Key inclusion criteria**

1. Hospitalised for CAP
2. Uncomplicated CAP confirmed by physician
3. CURB65 score two or more
4. Aged 16 and over

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

16 years

### **Sex**

All

### **Total final enrolment**

25

### **Key exclusion criteria**

1. Immunodeficiency - defined as being on long term (28 days) oral prednisolone 10mg or more per day or other long-term disease-modifying drug
2. All forms of pulmonary fibrosis including usual interstitial pneumonia, asbestosis, non-specific interstitial pneumonia, hypersensitivity pneumonitis, active sarcoidosis
3. No capacity to consent

4. Active malignancy
5. Solid organ transplant
6. COPD on domiciliary oxygen therapy
7. Palliative treatment only
8. Mechanical ventilation
9. End of life care
10. Previously randomised into this trial
11. Participation in another CTIMP or CIMD interventional study

**Date of first enrolment**

27/05/2019

**Date of final enrolment**

31/03/2021

## **Locations**

**Countries of recruitment**

United Kingdom

England

Scotland

**Study participating centre**

**NHS Lothian**

Respiratory Medicine

Royal Infirmary Edinburgh

51 Little France Crescent

Edinburgh

United Kingdom

EH16 4SA

**Study participating centre**

**The Newcastle Upon Tyne Hospitals NHS Foundation Trust**

Freeman Hospital

Freeman Road

High Heaton

Newcastle-upon-Tyne

United Kingdom

NE7 7DN

**Study participating centre**

**Nottingham University Hospitals NHS Trust**

Trust Headquarters

Queens Medical Centre  
Derby Road  
Nottingham  
United Kingdom  
NG7 2UH

**Study participating centre**  
**University Hospital Southampton NHS Foundation Trust**  
Mailpoint 18  
Southampton General Hospital  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**University College London Hospitals NHS Foundation Trust**  
250 Euston Road  
London  
United Kingdom  
NW1 2PG

## **Sponsor information**

**Organisation**  
NHS Lothian

**ROR**  
<https://ror.org/03q82t418>

**Organisation**  
University of Edinburgh

**ROR**  
<https://ror.org/01nrxf90>

## **Funder(s)**

**Funder type**

Government

### Funder Name

National Institute for Health Research; Grant Codes: 2019/0032TMF

### Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### 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 analysed during the current study will be available upon request from the chief investigator Prof Adam Hill by emailing [pibcap@ed.ac.uk](mailto:pibcap@ed.ac.uk). Following publication of the primary paper, a de-identified individual participant data set will be submitted to data archiving for sharing purposes. Access to the de-identified dataset will be under a controlled access model in line with ECTU policies at that time.

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Protocol file</a>	version v3.0	12/03/2019	28/05/2019	No	No
<a href="#">Protocol file</a>	version 4.0	05/07/2019	01/12/2021	No	No
<a href="#">Protocol file</a>		26/11/2019	01/12/2021	No	No