ISRCTN42850134 https://doi.org/10.1186/ISRCTN42850134

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

Submission date
08/04/2019

Recruitment status
Stopped

Registration date
28/05/2019

Overall study status
Stopped

Last Edited
01/12/2021

Condition category
Respiratory

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

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

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 to request a patient information sheet

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 measure
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

Secondary outcome measures
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

Overall study start date
01/12/2017

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

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 843; UK Sample Size: 843

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
England

Scotland

United Kingdom

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

Sponsor details

c/o Kenneth Scott
The Queen’s Medical Research Institute
47 Little France Crescent
Edinburgh
Scotland
United Kingdom
EH16 4TJ
+44 (0)1312423325
accord@nhslothian.scot.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.nhslothian.scot.nhs.uk/Pages/default.aspx

ROR
https://ror.org/03q82t418

Organisation
University of Edinburgh

Sponsor details
c/o Fiach O'Mahony
Queens Medical Research Institute
47 Little France Crescent
Edinburgh
Scotland
United Kingdom
EH16 4TJ
+44 (0)1312426226
fiach.o'mahony@ed.ac.uk

Sponsor type
University/education

Website
http://www.ed.ac.uk/home

ROR
https://ror.org/01nrxwf90

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

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. A lay version of the study results will be provided to the British Lung Foundation for dissemination

The protocol will be available on the trial website https://www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies
Any other study documentation (e.g. PIL) can be made available by emailing pibcap@ed.ac.uk
The SAP will be finalised before database lock, and can be requested by emailing pibcap@ed.ac.uk

Intention to publish date
31/03/2023

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. 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?
	version v3.0				

Protocol file	version 4.0	12/03/2019	28/05/2019	No	No
Protocol file		05/07/2019	01/12/2021	No	No
Protocol file		26/11/2019	01/12/2021	No	No
HRA research summary			28/06/2023	No	No