Can better tests improve the right use of antibiotics in respiratory infections?

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
22/05/2019		[_] Protocol		
Registration date 18/07/2019	Overall study status Completed	Statistical analysis plan		
		[_] Results		
Last Edited 18/07/2019	Condition category Respiratory	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 antibiotic therapy by 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.

We have developed a molecular test that identifies the cause of pneumonia in 87% of patients. Our test still works even if the patient has already started antibiotic treatment. Our test is very quick and we can have a result within a few hours. We call our test a "MICAP" molecular investigation of community acquired pneumonia.

The main aim of the study is to determine if the PIB CAP test can reduce the amount of antibiotics prescribed without any undesirable clinical side effects. We will count up how much antibiotic treatment each participant had, including any additional antibiotics that might have been needed after initial treatment.

Who can participate?

Any patient at the hospital over 18 years of age who has three or more of the symptoms of lower respiratory tract infection can participate.

What does the study involve?

We will invite patients who have been admitted to hospital with lower respiratory tract infection to enrol onto our study. We will use a computer program to randomly decide which test participants will have. Half the participants will have the usual NHS tests and will receive the

normal treatment for pneumonia. The other half of participants will have our molecular test and the results will customise their antibiotic treatment. We estimate that we will need to enrol 600 participants to the study in order to detect any differences between the group receiving standard NHS treatment and the group receiving customised antibiotic treatment. After 30 days each participant will have medical examinations and tests to see if it is safe to treat pneumonia with less antibiotics. We will also calculate if personalised antibiotic therapy is cost-effective for the NHS compared to the current treatment.

What are the possible benefits and risks of participating?

Benefits: guide to the best treatment for infection and limit the antibiotics to only those that are required for treatment

Risk: antibiotics that are not specific for treatment may have a benefit and these would not be provided to those taking part in the study

Where is the study run from? Royal Infirmary of Edinburgh, UK.

When is the study starting and how long is it expected to run for? June 2019 to June 2021

Who is funding the study? Chief Scientist Office, Division Scotland

Who is the main contact? Dr Kate Templeton, kate.templeton@ed.ac.uk

Contact information

Type(s) Public

Contact name Dr Kate Templeton

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Contact details Deparmtment of Medical Microbiology Royal Infirmary Edinburgh United Kingdom EH16 4SA 0131 242 6015 kate.templeton@ed.ac.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number Nil known

Secondary identifying numbers 246355

Study information

Scientific Title

Measuring the impact of improved diagnostics on antimicrobial stewardship in respiratory tract infection (MIDAS Study)

Acronym

MIDAS

Study objectives

The MICAP assay to diagnose the aetiological agents in CAP and LRTI will have a result within 36 hours of hospital admission and give personalised targeted antibiotic treatment safely reducing the antibiotic burden or giving the appropriate antibiotic based on the pathogen identified.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 24/08/2018 South East Scotland REC 1 (NHS Lothian, Waverley Gate, 2 - 4 Waterloo Place, Edinburgh, EH1 3EG; 0131 465 5473; Sandra.Wyllie@nhslothian.scot.nhs.uk), ref: 18/SS /0093, IRAS ID 246355

Study design Single centre randomised controlled trial

Primary study design Interventional

Secondary study design Randomised controlled trial

Study setting(s) Hospital

Study type(s) Diagnostic

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

Pneumonia, Lower respiratory tract infection

Interventions

Study arm (intervention arm) – patient sputum sample will be tested by rapid pneumonia assay (MICAP) and then have treatment guided in response to results. The treatment guidance is as per standard treatment based on NHS Lothian guidelines (available at https://www.ljf.scot.nhs.uk /LothianJointFormularies/Adult/5.0/(b)/Pages/default.aspx)

The control arm – receive standard microbiology investigations and treatment in accordance with NHS Lothian guidance.

Intervention Type

Device

Phase

Not Applicable

Primary outcome measure

To explore whether participants admitted with LRTI can safely receive personalised antibiotic therapy within 12 hours of consent for this test on existing sputum sample assessed by review of patient notes.

Secondary outcome measures

1. CAP resolution at days 7 and 30 (Y/N)

2. Major adverse events (Y/N) and number. Major adverse events = complicated parapneumonic effusion, empyema, lung abscess, vascular event (acute coronary syndrome or cerebrovascular accident) or antibiotic-associated C. difficile, need for inotropic support, non-invasive or invasive ventilation or another major adverse event reported by the clinician and confirmed by the adjudication committee

3. Readmissions to hospital within 30 days due to LRTI

4. Death (at 30 days and time to death)

5. Narrowing spectrum of antibiotics assessed by drug chart for antibiotics given daily from date of consent

6. Macrolide DDD assessed by drug chart for antibiotics given daily from date of consent

7. Alteration or addition of antibiotic therapy assessed by drug chart for antibiotics given daily from date of consent

8. Length of hospital stay assessed by date of admission to date of discharge. Recovered for hospital records

9. Antibiotic side effects measured from date of consent assessed by notes of side effects attributed to antibiotics in clinical notes

10. Antibiotic costs assessed by costs from Pharmacy unit of current drug costs for the course given

11. Patient symptoms assessed using a pneumonia specific questionnaire

12. Antibiotic resistance in bacteria isolated assessed by MICs of bacteria isolated, resistance markers via molecular methods for bacteria detected by PCR

13. Assess the optimum specimen(s) for assessment of LRTI for bacteria, atypical bacteria and Viruses assessed by comparison of PCR results with sputum to throat swab where they exist

14. Cost per Quality-Adjusted Life Year at 30 days

15. Cost per DDD of antibiotics at 30 days

Overall study start date 01/06/2019

Completion date

01/06/2021

Eligibility

Key inclusion criteria

 Aged 18 and over
 Hospitalised
 Lower respiratory tract specimen taken for routine microbiology within 48 hours of admission and - 3 or more of following signs or symptoms of respiratory tract infection:

 new or worsening cough
 new or worsening expectoration of sputum
 haemoptysis
 new or worsening dyspnea
 pleuritic chest pain
 fever
 headache
 abnormalities on chest auscultation or percussion

Participant type(s)

Patient

Age group Adult

Lower age limit 18 Years

Sex Not Specified

Target number of participants 600

Key exclusion criteria

1. Hospitalisation for more than 48 hours

2. No capacity to consent

3. Active malignancy

4. Immunodeficiency - defined as being on long term (28 days) oral prednisolone 10mg or more per day or other long term disease modifying drug

5. Solid organ transplant

6. All forms of pulmonary fibrosis including usual interstitial pneumonia, asbestosis, non-specific interstitial pneumonia, hypersensitivity pneumonitis, active sarcoidosis

7. Palliative treatment only

8. Mechanical ventilation

9. End of life care10. Previously randomised into this trial11. Participation in another CTIMP or CIMD interventional study

Date of first enrolment 22/07/2019

Date of final enrolment 31/01/2021

Locations

Countries of recruitment Scotland

United Kingdom

Study participating centre

Royal Infirmary of Edinburgh 51 Little France Crescent Edinburgh United Kingdom EH16 4SA

Sponsor information

Organisation NHS Lothian

Sponsor details

Research and Development Queens medical research Institute 47 Little France Crescent Edinburgh Scotland United Kingdom EH16 4TJ 0131 242 3330 kate.templeton@ed.ac.uk

Sponsor type Hospital/treatment centre

ROR https://ror.org/03q82t418

Funder(s)

Funder type Government

Funder Name Chief Scientist Office

Alternative Name(s) CSO

Funding Body Type Government organisation

Funding Body Subtype Local government

Location United Kingdom

Results and Publications

Publication and dissemination plan

Summaries of results will also be made available to Investigators for dissemination within their clinics (where appropriate and according to their discretion).

The data will be disseminated at local, national level via publication in peer review journals and at international meetings in Respiratory Medicine, Internal Medicine and Infectious Diseases. Results and links to study outputs will be available on the Laboratory medicine website http://www.edinburghlabmed.co.uk/ClinicalResearch/Pages/default.aspx

Intention to publish date

01/09/2021

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publically available repository (http://www.edinburghlabmed.co.uk/ClinicalResearch/Pages /default.aspx).

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No