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A study to evaluate diagnostic tests used at the point of care for improving antibiotic prescribing for patients with respiratory tract infections in primary care in Europe

Submission date
08/12/2020

Recruitment status
No longer recruiting

Registration date
11/12/2020

Overall study status
Completed

Last Edited
17/06/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
The development of antibiotics (such as penicillin) was a major breakthrough in medical science. Antibiotics are used to treat illness caused by bacteria. Development of these medicines meant that illnesses, like pneumonia, which were once often fatal, could now usually be successfully treated. However, the effectiveness of antibiotics is now decreasing because they are being overused. Bacteria that are being exposed to antibiotics can change genetically, making it harder for the antibiotics to work against them. As a result, “superbugs” are developing. There is no effective treatment for some of these “superbugs”. The development of resistance to antibiotics is a major public health concern worldwide. Using antibiotics too often and for the wrong illness increases antibiotic resistance.
Diagnostic tests used when a patient first visits their doctor (point of care diagnostic tests) could help identify patients that will and will not benefit from antibiotic treatment, and lead to better use of the precious medicines. This is especially true for community-acquired acute respiratory tract infections (CA-ARTI), such as sore throat or cough, the commonest acute reasons for antibiotics use in community care. This study will test whether having a diagnostic test result available when healthcare professions make a decision about antibiotic prescribing results in fewer antibiotics being prescribed without harming patients. The study will run in community care including doctor’s surgeries, paediatric centres or long-term care homes in several countries and will last for about 2 years. It is hoped that the results will improve care. The aim of the study is to determine if having a CA-ARTI diagnostic (CA-ARTI-Dx) test result available when a clinician is considering or intending to prescribe an antibiotic leads to more appropriate prescribing decisions without causing harm to patients.

Who can participate?
Anyone over 1 year old presenting to sites participating in the study with either a cough which started less than 28 days ago, or a sore throat which started less than 14 days ago, whose GP is considering or planning to prescribe antibiotics for their symptoms.

What does the study involve?
The patients' eligibility for the study will be checked. If eligible, the patient will be told all the details of the study and given the opportunity to ask questions, and if they are happy to take part they will be asked to provide written informed consent. A member of the clinical team will complete a short questionnaire by asking the patient some questions about their illness and review their medical history. If the patient has had symptoms for 5 days or less they will have a test for the coronavirus SARS-CoV-2. If positive for COVID-19 the patient will be managed according to the current NHS guidelines but will not be able to continue with the study. If they test negative or have had symptoms for more than 5 days they will continue to randomisation. The participant will be randomly allocated to usual care or a diagnostic test. If the participant is allocated to usual care the consulting clinician will complete the questionnaire and provide any treatment and advice for managing their illness following best practice and national guidelines. If the participant is allocated to a diagnostic test, a sample will be taken required for the diagnostic test and the test will be performed according to the manufacturer’s instructions. Once the test result is available the consulting clinician will complete the study questionnaire and provide any treatment and/or additional advice for managing the participant's illness. The participant will be provided with a paper or online 14-day diary and told how to complete it. At home the participant will complete the daily diary, this should take no more than 5 minutes each day. The study team will ring the participant on day 14 to 17 if they have not completed or returned the diary. The study team will ring the participant on or just after day 28 to ask them questions about their illness/recovery over the past two weeks. If the participant has consented to this they may be contacted to take part in an interview about their experience in this study and their thoughts on the use of diagnostics tests in the management of their symptoms.

What are the possible benefits and risks of participating?
By participating in this study participants may not personally benefit but they will help doctors learn more about which diagnostic tests could help them make better decisions when treating people with cough or sore throat. Participants will be helping with research that may lead to a more personalised approach to antibiotic prescribing, one that better targets antibiotics to patients who are likely to benefit and directs alternative non-antibiotic treatments to patients who are unlikely to benefit. There are no foreseen risks but if participants are allocated to usual care plus a diagnostic test, a biological sample will be taken. Depending on what type of sample, some discomfort may be felt. The consultation may take longer than it would normally take without a diagnostic test.

Where is the study run from?
The study is run from the Primary Care Clinical Trials Unit, part of the Nuffield Department of Primary Care Health Sciences, University of Oxford (UK). In each country there will be a co-ordinating centre who will run the study on behalf of the University of Oxford.

When is the study starting and how long is it expected to run for?
January 2020 to April 2024

Who is funding the study?
Innovative Medicines Initiative 2 Joint Undertaking (EU)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
285877

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 46894, IRAS 285877, Grant Codes: EC 820755, WT 217075/Z/19/Z - VALUE-Dx

Study information

Scientific Title
Platform randomised controlled trial of point of care diagnostics for enhancing the quality of antibiotic prescribing for community-acquired acute respiratory tract infection in ambulatory care in Europe

Acronym
PRUDENCE

Study objectives
The use of diagnostic tests for patients with community acquired acute respiratory tract infection will safely improve antibiotic prescribing to patients that need it

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/11/2020, North West – Liverpool Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8197; liverpoolcentral.rec@hra.nhs.uk), REC ref: 20/NW/0385

Study design
Pragmatic platform randomized controlled trial of point-of-care diagnostics

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Community-acquired acute respiratory tract infection

Interventions
This will be a multi-country, prospective, individually randomised, platform clinical trial in community care with a nested process evaluation. The trial will be a diagnostic strategy intervention study to evaluate the use of clinical algorithms/flowchart that include a CA-ARTI-Dx, compared to usual clinical care without CA-ARTI-Dx. The trial will initially be three-arm, comparing usual care (with the availability of local guidelines for managing infections) without CA-ARTI point of care testing (POCT) with two different diagnostic strategies using CA-ARTI-Dx POCTs.

The study has the capacity to drop a CA-ARTI-Dx via an interim analysis after the end of the first recruitment period, most likely after the first winter season if recruitment is as expected, based on pre-specified criteria for either success or futility. If a CA-ARTI-Dx is dropped, it may be replaced with a new CA-ARTI-Dx to be evaluated in the second recruitment period. The nested process evaluation will capture data to understand how CA-ARTI-Dx is used in practice and how it influences patient care and experience. These data will inform implementation within the period of the trial and beyond.

Study participants
Patients aged one year and older, presenting to primary care: with lower respiratory tract infection where cough is the predominant symptom (<28 days); OR upper respiratory tract infection where acute sore throat (<14 days) is the dominant symptom; AND for whom the responsible clinician is considering or has decided to prescribe an antibiotic.

Recruitment
Primary care healthcare workers will recruit participants through the recruiting sites which will be the first point of care for that participant (e.g. GP practice, primary care paediatric centres or Long-Term Care Facilities [LTCFs]). The study will include recruiting sites from up to 12 European Union and/or Horizon 2020 countries in the trial. Some countries may recruit only from GP practices or only from LTCF. In some countries, where clinicians attend patients in LTCFs, participating general practices will potentially include eligible patients whom they care for and who are resident in an LTCF.

Potential participants will be identified when they present to their recruiting site with symptoms of CA-ARTI. Potential participants will be referred for eligibility assessment and potential trial entry as soon as possible. They will consult with a responsible clinician or appropriately trained delegate, where they will have the trial presented to them and be screened to confirm whether or not they meet the eligibility criteria. If eligible and willing, they will be recruited into the trial.

Screening and eligibility assessment
Participants will be assessed against the eligibility criteria by the responsible clinician or delegate who will complete the eligibility CRF on paper or online, they will then go on to complete a baseline assessment. If there is a meaningful delay between the introduction of the study/initial eligibility assessment and consent/randomisation, then the responsible clinician must confirm that all eligibility criteria are still met.

Informed consent
Participants will be provided with a participant information leaflet and a member of the clinical team will discuss what the trial involves with them. Participants will be given time to think about whether they would like to take part in the study, they will be able to ring friends or family members if they wish to discuss taking part. If the participant agrees to take part, they will then be asked to complete a consent form. Instructions on how to fill out the form will be provided. An optional consent question will be included on whether they would like to be contacted by the research team to be invited to a telephone interview for the nested process evaluation.

For the nested process evaluation study, a participant information leaflet will be provided and verbal consent will then be sought from the study participants who are invited for an interview. Healthcare workers will also be given a participant information leaflet and will provide verbal consent prior to participating in the nested process evaluation interviews.

Initial questionnaire
A member of the clinical team will complete a short web-based questionnaire including some details about the participant and their symptoms. We will also collect some contact details such as name, email address and telephone number so that the trial team can contact the participant and ask them questions about their recovery.

Randomisation
Once the initial questionnaire is complete the clinical team member will enter the participant’s baseline data into the online system, which will then enable the randomisation to take place. The randomisation process will take only a few moments via the online system and will not delay trial participation. The clinician will discuss the result of the randomisation with the participant.

Participant randomised to usual care
Clinicians will provide the treatment and advice for managing the participant's illness as they would normally do i.e. as if they were not taking part in the study.

Participant randomised to a diagnostic test
If a participant is randomised to the diagnostic test group, a member of the clinical team will take a sample from the participant. This could be a swab from the participant's nose or mouth, or a pinprick of blood from their finger, depending on the test they have been randomised to. The clinical team member will perform the diagnostic test, which varies according to the nature of the test but is usually no more than 20 minutes. Once the test result is ready, the clinician will discuss their recommended treatment and offer any additional advice for managing the participant's illness.

Samples
Samples will only be taken from the participant for study purposes if they are randomised to having a diagnostic test. The samples will be handled and processed according to the diagnostic test instructions and any leftover sample will be destroyed.

Follow-up
The clinical team will give the participant a paper diary or link to an online diary. They will go through the diary with the participant, explain how to complete it and answer any questions. The participant will be asked to complete the diary for 14 days starting on the day of consultation for this illness. It should take no more than five minutes to complete the diary each day.

The diary will include questions about the participant's illness, recovery, healthcare use, out-of-pocket expenditure, time off work or school, quality of life, satisfaction with the initial consultation, beliefs about the need for antibiotics for respiratory symptoms and your thoughts on managing symptoms in the future.

If the trial team have not received the completed daily diary after 14 - 17 days, they will ask the participant a brief set of questions, similar to those asked in the diary, by telephone. The participant will also be called on or just after day 28, the last day of the follow-up period, to ask a brief set of questions about the final two weeks of their illness/recovery.

Each telephone call will last no more than 5 minutes. The trial team will make up to three attempts to call the participant on each occasion. The trial team may send text reminders to complete the daily diary. However, the participant will have the opportunity to opt-out of this if they wish. The study team may access the participant's medical records to collect information on any hospitalisations during the follow-up period.

A mixed-methods process evaluation will be nested within the trial. The process evaluation will capture data to understand how the intervention is used and viewed by clinicians and patients in order to explain how clinicians and patients adopt CA-ARTI-Dx in community care. Interviews with a subset of both participants in the trial and healthcare workers will be carried out. Additionally, surveys will assess the views of clinicians and patients on the use of CA-ARTI-Dx in ARTI consultations, examine how CA-ARTI-Dx are implemented and experienced.

Intervention Type
Other

Primary outcome(s)
Co-primary outcome:
The proportion of participants being prescribed at least one antibiotic course (of any dose or duration) over 28 days from inclusion (estimating possible reduction) and time to return to usual daily activities, where returned to usual daily activity = yes (estimating non-inferiority), measured on day 1 – 14 using paper/online diary or Day 14 telephone call, and Day 28 telephone call

Key secondary outcome(s))
1. Choice of antibiotic class, whether ‘delayed’ or immediate measured on day 1 – 14 using paper /online diary or day 14 telephone call, and 28 telephone call
2. Antibiotic use over 28 days after inclusion measured on day 1 – 14 using paper/online diary or day 14 telephone call, and 28 telephone call
3. Patient-reported symptoms severities, re-consultations, hospitalization, pneumonia measured

on day 1 – 14 using paper/online diary or day 14 telephone call, and day 28 telephone call
4. Use of other, non-antibiotic, medication including antiviral medication, and over-the-counter treatments measured on day 1 – 14 using paper/online diary or day 14 telephone call, and day 28 telephone call
5. Responsible clinician's initial working diagnosis and antibiotic prescribing decision before test, if randomised to CA-ARTI-Dx also final decision after test, measured using online CRF at the baseline visit
6. Patient Enablement Instrument (PEI) score measured using the paper/online diary on day 1
7. Costs data: EQ5D at day 1, day 14 and day 28; time taken for testing; costs associated with subsequent help-seeking, complications, work loss and over-the-counter medication use (to be determined in close collaboration with WP5); measured using paper/online diary or day 14 telephone call, and day 28 telephone call

Completion date
30/04/2024

Eligibility

Key inclusion criteria
1. Male or female, aged 1 year and older
2. Consulting with symptoms of lower respiratory tract infection where cough is the predominant symptom (<28 days); or, symptoms of an upper respiratory tract infection (<14 days) where a sore throat is the dominant symptom; and where the clinician is considering/has decided to prescribe an antibiotic
3. Is able and willing to comply with all trial requirements
4. Participant or legal guardian(s) of a child is willing and able to give informed consent according to national regulations

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
1 years

Sex
All

Total final enrolment
2649

Key exclusion criteria
1. Patients with only nasal, ear or rhinosinusitis symptoms
2. Patients who have tested positive to SARS-CoV-2 within 28 days of onset of symptoms
3. Patients with any serious condition associated with immunocompromised (long term oral

steroids or immunosuppressants, terminal cancer)
4. Patients for whom the clinician decides on immediate hospital admission
5. Patients who will not be able to participate in the study because they do not understand the local language; are terminally ill; have a serious psychiatric disorder; or judgement of the recruiting clinician deems ineligible

Date of first enrolment
01/09/2021

Date of final enrolment
25/01/2024

Locations

Countries of recruitment
United Kingdom

England

Wales

Belgium

France

Georgia

Germany

Greece

Hungary

Ireland

Israel

Italy

Poland

Spain

Switzerland

Study participating centre
NIHR CRN: Thames Valley and South Midlands
John Radcliffe Hospital
Headley Way
Headington

Oxford
United Kingdom
OX3 9DU

Study participating centre
Cardiff & Vale University LHB
Woodland House
Maes-Y-Coed Road
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CF14 4HH

Study participating centre
Cwm Taf Morgannwg University Local Health Board
Dewi Sant Hospital
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
European Commission

Alternative Name(s)
European Union, Comisión Europea, Europäische Kommission, EU-Kommissionen, Euroopa Komisjoni, EC, EU

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		17/06/2025	17/06/2025	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version V2.0	28/10/2020	11/12/2020	No	Yes
Protocol file	version V2.0	28/10/2020	11/12/2020	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes