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Development of a point-of-care antibiotic susceptibility test for urinary tract infections

Submission date
23/08/2023

Recruitment status
No longer recruiting

Registration date
29/09/2023

Overall study status
Completed

Last Edited
29/09/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
In England, NHS hospitals spend £400 million per year treating urinary tract infections (UTIs). Based on clinical diagnosis in conjunction with the result of the urine dipstick test, doctors usually prescribe a broad-spectrum antibiotic (one that is effective against many types of bacteria). However, of those people diagnosed with UTIs, antibiotics are prescribed for 34-60% of them before their diagnosis can be confirmed by the laboratory. To identify the specific bacteria causing the infection, a urine specimen needs to be sent to a laboratory where it is grown and tested to determine which antibiotic would be most effective against it. It takes 1-3 days to obtain results, and samples aren't taken from all patients. This overuse of broad-spectrum antibiotics has led to the emergence of bacteria that are resistant to several antibiotics and can also put patients at risk of infection from "super bacteria".
The data generated during this research will be used to develop and evaluate a rapid, portable test that checks for antibiotic drug resistance in bacteria responsible for UTIs so that clinicians can treat the infection with the most appropriate antibiotic drug, maximising the likelihood that the infection will be cleared.

Who can participate?
Adults over the age of 18 years with a suspected UTI

What does the study involve?
The clinical team will ask for a urine sample which will be analysed in the lab as part of routine care. Researchers will take a small amount of the sample to help the development of the novel antibiotic susceptibility test. The sample will be tested in an NHS site and destroyed after the test is complete. The rest of the sample will be processed as normal. Researchers will also collect data such as demographics and medical information to help analyse the data from the urine sample. The data collected in the questionnaire and information from patient records will be kept anonymously in the study database. The personal information will include name, age, email address, information about symptoms and general health. The participant does not have to do anything else after the sample has been taken.

What are the possible benefits and risks of participating?
Participating in this study will not affect the care participants receive.

Where is the study run from?
The study is run from the University of Reading and Hampshire Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
April 2022 to March 2025

Who is funding the study?
National Institute for Health and Care Research (UK)

Who is the main contact?
Dr Alexander Edwards, a.d.edwards@soton.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
316558

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
NIHR203362, IRAS 316558

Study information

Scientific Title

Point-of-care antibiotic susceptibility testing to aid urinary tract infection treatment using dip-and test microcapillary devices

Acronym
POC AST UTI

Study objectives
Can we use a new direct from urine antibiotic susceptibility tests to provide rapid, accurate measurements of antibiotic susceptibility?

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/10/2022, Berkshire Research Ethics Committee (Level 3, Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)1173421389; berkshire.rec@hra.nhs.uk), ref: 22/SC/0393

Study design
Prospective non-interventional case-control study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Urinary tract infections

Interventions
This project will develop and evaluate a rapid, portable test that checks for antibiotic drug resistance in bacteria responsible for urinary tract infections (UTIs) directly from a patient's urine sample.

This is a prospective, non-interventional versus standard care study.

The researchers will compare the antibiotic susceptibility test results and the time to result obtained by the direct test developed in this study and tests used in standard care.

This study is planned for 3 years with two sample recruitment phases:
PHASE 1: development sample recruitment – 100 urine samples
600 remnant material urine samples
PHASE 2: prototype design (no sample recruitment)
PHASE 3: evaluation sample recruitment – 500 urine samples
Informed consent will be sought at phase 1 and phase 3 for fresh urine samples to collect questionnaire information and information from the patient record. Urinary tract infections are complex and patient factors such as age, catheterisation and pregnancy and have an impact on the test. For this reason, patient information will be collected to identify if there is a patient group (elderly, males, pregnancy) that causes significant negative effects on the test.

Recruitment of patients will not be continuous through the two recruitment phases. Testing of urine samples will be performed by research staff at the hospital sites. Recruitment will follow targeted recruitment times allowing approximately 20 samples a week to be recruited for testing. Following each recruitment week there will be a break in recruitment to allow analysis of data and review of antibiotic resistance prevalence until the required number of samples have been recruited. We will not be recruiting fresh patient samples during phase 2 of the project during the design phase.

Recruitment will be led by the clinical team. During recruitment times leaflets underlining the key identification and participant inclusion/exclusion criteria will be distributed to clinicians. Patients in the emergency department or inpatients can be recruited. If a patient has been identified as eligible, a member of the direct care team, the direct care team will ask them if they are happy to be approached by a member of the study clinical team and will give them a participant information sheet, and informed consent and questionnaire. This can happen before or after a urine sample has been collected but must be before the sample has been transferred to a boric acid container and any remaining urine discarded.
For standard care pathways the urine sample is transferred into a red top boric acid container or plain universal for standard analysis. Any remaining urine from these samples is poured into a plain 20 mL universal and stored at 4 C. The test can be processed with as little as 1 mL of leftover urine. Once the urine sample is collected, the research team is notified and the sample is taken for testing. We aim to process urine samples within 4 h of collection.
Sample Storage: After informed consent has been given, the clinical team will save any leftover urine sample (at least 1 ml) in a sterile 20 ml universal container and store it at 4oC. The research team from the University of Reading will be contacted and informed there is a sample to test. The researchers aim to test urine samples within 4 h of collection.

Sample size rationale:
The number of samples for analysis of qualitative antibiotic susceptibility tests, according to ISO20776-2 Clinical laboratory testing and in vitro diagnostic test system-Susceptibility testing of infectious agents and evaluation of the performance of antimicrobial susceptibility test devices, is 100. The samples should also have an even distribution of resistant and susceptible bacteria to calculate accuracy. The antibiotics tested have an estimated range of resistance of 1-70% (based on antibiotic resistance screening studies) with frontline antibiotics to be tested having the lowest resistance rates. For this reason, we will need to test over 100 samples for each phase of the study and test and store bacterial isolates from remnant urine material for supplemental testing to ensure a mix of resistance profiles for each antibiotic.
For antibiotics with the lowest resistance levels (1% range) practical limitations may limit the number of resistant samples and isolates that can be tested (i.e. five samples with resistant infection out of 500 participants); for these antibiotics as many samples will be collected as possible given practical limits (number of prototype tests produced, funding constraints). For this reason the researchers will also use diagnostic remnant samples to supplement these results. These samples will not have patient information and informed consent will not be collected. These samples will be used to supplement testing for example, since most infections are caused by Gram-negative E. coli, these samples will be used to collect more Gram-positive bacteria.

The researchers will collect urine from participants presenting with suspected UTI, however, not all of these participants will have a clinically confirmed urinary tract infection, and the bacterial load, species, and antibiotic susceptibility profile will be unknown at the point of recruitment and collection. Non-infected urine samples will be equally valuable for device development as these will provide essential baseline measurements to identify accuracy for determining infection vs non-infection.

For this reason the researchers expect to recruit:
PHASE 1: 100 urine samples for the development phase
PHASE 3: 500 urine samples for the evaluation phase.
PHASE 1-3: 600 remnant material urine samples

Patient information collection and storage:
Patient Information will be handled by the clinical team. Once consent has been obtained, data recorded in the patient record and the questionnaire will be transcribed by the clinical staff. This will include demographics, admission reason, clinical presentation, current medication record, specifically antibiotics and urinalysis information such as white cell count (WCC), bacterial count, isolate ID, and phenotype. During the study, the data will be pseudo-anonymised in the REDCap database.

Pseudo-anonymisation:
Urine samples will be anonymised by the clinical team. Urine samples will be labelled with a participant code. During the study, this sample collection and labelling will be linked to a recruitment log that can be linked to the participant to gain access to the correct patient records. Patient data from the patient record and questionnaire will be inputted into the REDCap database using the de-identified participant ID. Participants will only be recorded by their participant ID in the study database. Only the recruitment log will contain the patient ID and participant ID and this identifiable data will be retained on an NHS computer and password protected. The purpose of this recruitment log is purely to be able to correctly link clinical information and laboratory microbiology test results with the experimental test data, so that the de-identified study database can be kept as complete and accurate as possible. At the end of the study, and once all data has been collected and checked for accuracy, this participant log will be destroyed. Anonymised data will be stored long-term using REDCap for the preparation of reports and further analysis. Upon publication of findings, the underlying data sets should be made available in a public repository, subject to checks for any patient-identifiable data and compliance with all appropriate data collection legislation.
The clinical team at HHFT will have access to the patient record. The University of Reading team will have access to the anonymised information for analysis. After the end of the study, the participant log will be deleted and all data will be made fully anonymised.

Participant confidentiality:
Participant information will remain confidential. All samples and patient data will be referred to using a de-identified participant ID. The study database (REDCap) will be password-protected and only accessible to the research team. The study database will not contain any patient identifiers.
Hard copies of consent forms and questionnaires will be stored securely for the lifetime of the project at the NHS site.
The study will comply with the Data Protection Act 2018.
Study findings and study data will only be published following review to check for any potentially identifiable participant information.

Reporting:
The results will be analysed periodically throughout the sample recruitment period to monitor the antibiotic resistance rates of samples. For some antibiotics where resistance is more common, we expect to reach a statistically valid number of resistant and susceptible samples earlier than other, less common resistance profiles. Therefore, recruitment will continue if possible until we have enough samples with the least common resistance phenotypes. Once a sufficient number of samples with all relevant resistance phenotypes, the recruitment period may be ended to ensure the recruitment of only the required number of participants.

Researchers undertaking the development and evaluation of the new test will not know the results of the routine microbiology testing or patient information before reporting results, to minimise researcher bias. Reports will be produced quarterly for review by the research steering committee and PPIE study representatives.

Intervention Type
Device

Phase
Not Applicable

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

Primary outcome(s)
Antibiotic resistance of bacteria present in a urine sample, measured in a microfluidic antibiotic susceptibility test and compared to the clinical/reference result at a single timepoint

Key secondary outcome(s))
The time to detection of bacteria present in a urine sample in a microfluidic antibiotic susceptibility test, recorded over 24 hours

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. >18 years old
2. Suspected urinary tract infection as assessed by a clinician
3. Able to give informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

1. <18 years old
2. Too ill that taking informed consent would disrupt care
3. Unable to give informed consent

Date of first enrolment
01/09/2023

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Hampshire Hospitals NHS Foundation Trust
Basingstoke and North Hampshire Hos
Aldermaston Road
Basingstoke
United Kingdom
RG24 9NA

Sponsor information

Organisation
University of Reading

ROR
https://ror.org/05v62cm79

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

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 data-sharing plans for the current study are unknown and will be made available at a later date. Participant data will be de-identified and only anonymous data will be published.

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